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(21) International Application Number: PCT/US97/22787 (22) International Filing Date: 11 December 1997 (11.12.97) (30) Priority Data: 60/032,757 11 December 1996 (11.12.96) US (71) Applicant: CHIRON CORPORATION [US/US]; 4560 Horton Street, Emeryville, CA 94608 (US). (72) Inventors: ESCOBEDO, Jaime; 1470 Livorna Road, Alamo, CA 94507 (US). HU, Quianjin; Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608 (US). GARCIA, Pablo; 882 Chenery Street, San Francisco, CA 94131 (US). WILLIAMS, Lewis, T.; 3 Miraflores Lane, Tibouron, CA 94920 (US). KOTHAKOTA, Srinivas; Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608 (US). (74) Agents: POTTER, Jane, E., R.; Chiron Corporation, Intellectual Property - R440, P.O. Box 8097, Emeryville, CA 94662-8097 (US) et al.		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: SECRETED HUMAN PROTEINS		
(57) Abstract Secreted proteins can be identified using a method which exploits the ability of microsomes to modify proteins post-translationally. Nineteen human secreted proteins and full-length cDNA sequences encoding the proteins have been identified using this method. The proteins and cDNA sequences can be used, <i>inter alia</i> , for targeting other proteins to the membrane or extracellular milieu.		

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SECRETED HUMAN PROTEINS

5 This application claims the benefit of copending provisional application
Serial No. 60/032,757, filed December 11, 1996, which is incorporated herein by
reference.

TECHNICAL AREA OF THE INVENTION

10 The invention relates to the area of proteins. More particularly, the
invention relates to human secreted proteins.

BACKGROUND OF THE INVENTION

15 Secreted proteins include such important proteins as growth factors,
cytokines and their receptors, extracellular matrix proteins, and proteases.
Nucleotide sequences encoding these proteins can be used to detect disease states in
which such proteins are implicated and to develop therapeutics for such diseases.
Thus, there is a need in the art for methods of identifying secreted proteins and the
nucleotide sequences which encode them.

SUMMARY OF THE INVENTION

20 It is an object of the invention to provide an isolated and purified human
protein.

It is yet another object of the invention to provide a fusion protein.

It is still another object of the invention to provide a preparation of antibodies.

It is even another object of the invention to provide an isolated and purified subgenomic polynucleotide.

5 It is yet another object of the invention to provide an isolated gene.

It is a further object of the invention to provide a DNA construct for expressing all or a portion of a human protein.

It is still another object of the invention to provide a host cell comprising a DNA construct.

10 It is another object of the invention to provide a homologously recombinant cell.

It is even another object of the invention to provide a method of producing a human protein.

15 It is another object of the invention to provide a method of identifying a secreted polypeptide which is modified by rough microsomes.

These and other objects of the invention are provided by one or more of the embodiments described below.

20 One embodiment of the invention provides an isolated and purified human protein. The isolated and purified human protein has an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

25 Another embodiment of the invention provides an isolated and purified human protein having an amino acid sequence which is at least 85% identical to an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

30 Still another embodiment of the invention provides a polypeptide comprising at least 6 contiguous amino acids of an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

Even another embodiment of the invention provides a fusion protein. The fusion protein comprises a first protein segment and a second protein segment fused together by means of a peptide bond. The first protein segment consists of at least 6 contiguous amino acids selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

Yet another embodiment of the invention provides a preparation of antibodies. The antibodies specifically bind to a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

Even another embodiment of the invention provides an isolated and purified subgenomic polynucleotide. The isolated and purified subgenomic polynucleotide has a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

Yet another embodiment of the invention provides an isolated and purified subgenomic polynucleotide consisting of at least 10 contiguous nucleotides selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

Still another embodiment of the invention provides an isolated gene. The isolated gene corresponds to a cDNA sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

Another embodiment of the invention provides a DNA construct for expressing all or a portion of a human protein. The DNA construct comprises a promoter and a polynucleotide segment. The polynucleotide segment encodes at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

The polynucleotide segment is located downstream from the promoter.

Transcription of the polynucleotide segment initiates at the promoter.

Even another embodiment of the invention provides a host cell comprising a DNA construct. The DNA construct comprises a promoter and a polynucleotide segment. The polynucleotide segment encodes at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. The polynucleotide segment is located downstream from the promoter. Transcription of the polynucleotide segment initiates at the promoter.

Still another embodiment of the invention provides a homologously recombinant cell having incorporated therein a new transcription initiation unit. The transcription initiation unit comprises in 5' to 3' order an exogenous regulatory sequence, an exogenous exon, and a splice donor site. The transcription initiation unit is located upstream to a coding sequence of a gene. The gene comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19. The exogenous regulatory sequence controls transcription of the coding sequence of the gene.

Yet another embodiment of the invention provides a method of producing a human protein. A culture of a cell is grown. The cell comprises a DNA construct. The DNA construct comprises a promoter and a polynucleotide segment. The polynucleotide segment encodes at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. The polynucleotide segment is located downstream from the promoter. Transcription of the polynucleotide segment initiates at the promoter. The protein is purified from the culture.

Even another embodiment of the invention provides a method of producing a human protein. A culture of a cell is grown. The cell comprises a new transcription initiation unit. The transcription initiation unit comprises in 5' to 3'

order an exogenous regulatory sequence, an exogenous exon, and a splice donor site. The transcription initiation unit is located upstream to a coding sequence of a gene. The gene comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19. The exogenous regulatory sequence controls transcription of the coding sequence of the gene. The protein is purified from the culture.

Another embodiment of the invention provides a method of identifying a secreted polypeptide which is modified by rough microsomes. A population of cDNA molecules is transcribed *in vitro* whereby a population of cRNA molecules is formed. A first portion of the population of cRNA molecules is translated *in vitro* in the absence of rough microsomes whereby a first population of polypeptides is formed. A second portion of the population of cRNA molecules is translated *in vitro* in the presence of rough microsomes whereby a second population of polypeptides is formed. The first population of polypeptides is compared with the second population of polypeptides. Polypeptide members of the second population which have been modified by the rough microsomes are detected.

The present invention thus provides the art with a method for identifying secreted proteins or polypeptides, the amino acid sequences of nineteen novel human secreted proteins, and the nucleotide sequences which encode these proteins. The invention can be used to, *inter alia*, to produce secreted proteins for therapeutic and diagnostic purposes.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The inventors have discovered a method for identifying secreted proteins or polypeptides. Secreted proteins or polypeptides include soluble proteins which can be transported across a membrane, such as a cell membrane, nuclear membrane, or membrane of the endoplasmic reticulum, as well as proteins which can be partially secreted from a cell, such as membrane-bound receptors.

Secreted proteins can contain a signal (or secretion leader) sequence, located at the N-terminus and including at least several hydrophobic amino acids,

such as phenylalanine, methionine, leucine, valine, or tryptophan. Non-hydrophobic amino acids can also be included in the signal sequence. Signal sequences are described in von Heijne, *J. Mol. Biol.* 184:99-105 (1985) and Kaiser and Botstein, *Mol. Cell. Biol.* 6:2382-2391 (1986). Secreted proteins can also be glycosylated by post-translational modification. The presence of a signal sequence or the presence of glycosylation or both indicate that a particular protein is a secreted protein.

In order to identify secreted proteins or polypeptides, the method of the invention exploits properties of microsomes, which are the closed vesicles that result from fragmentation of endoplasmic reticulum. Microsomes can be rough or smooth, depending on whether the endoplasmic reticulum from which they were derived is studded with ribosomes. Microsomes, particularly rough microsomes, have the ability to perform post-translational modifications, such as glycosylation and cleavage of signal sequences from proteins or polypeptides.

To identify secreted proteins, a population of complementary DNA (cDNA) molecules is transcribed *in vitro* to synthesize a population of complementary RNA (cRNA) molecules. The cDNA molecules can be synthesized by reverse transcription of mRNA molecules isolated from a particular cell or tissue type or organism using, for example, a commercially available reverse transcriptase enzyme. Alternatively, the reverse transcription reaction to form cDNA molecules can be conducted on total RNA, without a preliminary purification of mRNA.

Any organism, such as a bacterium, plant, invertebrate, or vertebrate organism, can be used as a source of RNA. Particularly preferred sources of RNA are mammals, most preferably humans. Tissues, such as liver, brain, kidney, spleen, pancreas, or muscle, can be used as a source of RNA. Individual cell types, either primary cells or members of established cell lines, such as HeLa, CHO, PC12, P19, BHK, COS, or HepG2, are suitable sources of RNA. Tissues or primary cells isolated from organisms at a particular stage in development can be used as RNA sources. Stem cells, such as hematopoietic, neuronal, and embryonic stem cells, can also be used as a source of RNA.

Total RNA or mRNA can be isolated using methods known in the art. Such methods are described, *inter alia*, in Sambrook *et al.*, MOLECULAR CLONING, A

LABORATORY MANUAL (2d ed., Cold Spring Harbor Press, N.Y., 1989), and Ausubel *et al.*, CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (Greene Publishing Associates and John Wiley & Sons, N.Y., 1994). Techniques for RNA isolation can be tailored for a particular organism or cell type, as is known in the art.

5 Complementary DNA can optionally be obtained from a cDNA library. The cDNA library can be derived from the genome of any organism of interest, particularly a mammal or a human. Tissue- or cell type-specific cDNA libraries can also be used as a source of cDNA.

10 Transcription of cDNA molecules *in vitro* to form cRNA molecules can be carried out using any methods known in the art. These methods include, for example, placing cDNA into a cloning vector containing a promoter, such as an SP6, T7, or T3 polymerase promoter, and transcribing the cDNA using the appropriate polymerase. A variety of commercial kits are available for this purpose.

15 A first portion of the population of cRNA molecules can be translated *in vitro*, in the absence of rough microsomes, to form a first population of polypeptides which have not been post-translationally modified. A second portion of the population of cRNA molecules can be translated *in vitro* in the presence of rough microsomes. Under the conditions of the *in vitro* translation reaction, rough microsomes can cleave signal sequences from those polypeptides which comprise
20 such sequences. Under the same conditions, rough microsomes can also glycosylate those polypeptides which contain glycosylation sites.

25 Methods of *in vitro* translation are those which are known in the art, such as translation in a reticulocyte lysate system, particularly a rabbit reticulocyte lysate. Reticulocyte lysate systems can be assembled in the laboratory or purchased commercially in kit form.

30 Microsomes can be prepared by disruption of tissues or cells by homogenization, as is known in the art. If desired, rough and smooth microsomes can be separated using well-known techniques, such as sucrose density gradient sedimentation. Microsomes are also available commercially, for example, such as the canine pancreatic microsomes available from Promega Corp., Madison, WI.

The first population of polypeptides can then be compared with the second population of polypeptides. This comparison can be by means of, for example, one- or two-dimensional polyacrylamide gel electrophoresis, as is known in the art. Polypeptides separated in the gels can be detected by any means known in the art, such as staining with copper, silver, Coomassie Brilliant Blue, amido black, fast green FCF, Ponceau S, or a chromophoric label. Separated proteins can also be visualized using radioactive, chemiluminescent, fluorescent, or enzymatic tags incorporated into the proteins before separation.

The gels can be dried or the proteins can be transferred to membranes, such as polyvinylidene difluoride membranes. Either the gels or membranes themselves or photographs of the gels or membranes can be compared by eye. Alternatively, the gels or membranes can be scanned, for example, with a densitometer and analyzed with the aid of a computer.

Polypeptide members of the second population of polypeptides, which have been modified by the rough microsomes, can be detected by any means available in the art. For example, a shift in the position of a polypeptide band can be observed, indicating an increase in molecular weight of a member of the second population compared with the corresponding polypeptide member of the first population. Such an increase in molecular weight indicates that the polypeptide member of the second population was glycosylated by the rough microsomes.

A shift in the position of a polypeptide band indicating a decrease in molecular weight of a member of the second population compared with the corresponding polypeptide member of the first population can also be observed. This decrease in molecular weight indicates that the polypeptide member of the second population contained a signal sequence which was cleaved by the rough microsomes.

Polypeptides which are modified by the rough microsomes are identified as secreted polypeptides. Optionally, quantities of cDNA molecules which encode secreted polypeptides can be obtained. Molecules of cDNA which encode polypeptides which are post-translationally modified by the rough microsomes can be placed into suitable vectors using standard recombinant DNA techniques and

used to transform host cells. Many vectors are available for this purpose, such as retroviral or adenoviral vectors and bacteriophage, as described below.

Vectors comprising cDNA which encode secreted polypeptides can be introduced into host cells using techniques available in the art. These techniques include, but are not limited to, transferrin-polycation-mediated DNA transfer, transfection with naked or encapsulated nucleic acids, liposome-mediated cellular fusion, intracellular transportation of DNA-coated latex beads, protoplast fusion, viral infection, electroporation, and calcium phosphate-mediated transfection.

The host cells can be any host cells which are capable of propagating cDNA molecules. A variety of host cells, for example immortalized cell lines such as HeLa, CHO, or HEK, are available for this purpose.

Transformed host cells can be diluted serially and cultured to form individual colonies. Methods of culturing host cells and the media suitable for each host cell type are well known in the art. Preferably, each colony originates from a single transformed host cell. Separate preparations of cDNA from each colony can be prepared, as described above, and transcribed *in vitro* to form cRNA. The cRNA can be transcribed to form secreted polypeptides, which can be purified as is known in the art. If the preparation of secreted polypeptides from a colony contains more than one species of polypeptide, the steps described above can be repeated until a colony is obtained which contains cDNA encoding only a single species of polypeptide.

Complementary DNA molecules which encode secreted proteins can be sequenced using standard nucleotide sequencing techniques. The sequence of each cDNA molecule can be compared with known sequences in a database to determine whether the clone encodes a known or a novel secreted protein.

The inventors have used the method of the invention to identify nineteen novel human secreted proteins. Amino acid sequences for these nineteen human secreted proteins are disclosed in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. Nucleotide sequences which encode the proteins are disclosed in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19, respectively.

Clones containing the cDNAs of the secreted proteins were deposited on December 11, 1997, with the ATCC. Individual bacterial cells (*E. coli*) in this composite deposit contain one or more of the polynucleotides encoding the secreted proteins of the invention and can be retrieved using an oligonucleotide probe designed from the sequence for that particular polynucleotide, as provided herein. Each polynucleotide can be removed from the vector by performing an EcoRI/NotI digestion (5' site, EcoRI; 3' site, NotI). The deposit submitted to the ATCC has been designated SECP120997. The nucleotide sequences of these deposits and the amino acid sequences they encode are controlling in the event of a discrepancy between the amino acid and nucleotide sequences disclosed herein and those contained in the deposits.

A purified and isolated subgenomic polynucleotide of the present invention comprises at least 10, 12, 15, 18, 20, 25, 30, 35, 40, 45, or 50 contiguous nucleotides selected from the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19. The isolated and purified subgenomic polynucleotides can comprise an entire nucleotide sequence selected from the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

Subgenomic polynucleotides contain less than a whole chromosome and are preferably intron-free. Polynucleotides of the invention can be isolated and purified free from other nucleotide sequences by standard nucleic acid purification techniques, using restriction enzymes and probes to isolate fragments comprising the coding sequences.

Isolated genes corresponding to the cDNA sequences disclosed herein are also provided. Known methods can be used to isolate the corresponding genes using the provided cDNA sequences. These methods include preparation of probes or primers from the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 for use in identifying or amplifying the genes from human genomic libraries or other sources of human genomic DNA.

The coding sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 can be made using reverse transcriptase with

human mRNA as a template. Amplification by PCR can also be used to obtain the polynucleotides, using either genomic DNA or cDNA as a template. Polynucleotide molecules of the invention can also be made using the techniques of synthetic chemistry given the sequences disclosed herein. The degeneracy of the genetic code permits alternate nucleotide sequences which will encode the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38 to be synthesized. All such nucleotide sequences are within the scope of the present invention.

Polynucleotide molecules of the invention can be propagated in vectors and cell lines as is known in the art. Polynucleotide molecules can be on linear or circular molecules. They can be on autonomously replicating molecules or on molecules without replication sequences. For propagation, polynucleotides of the invention can be introduced into suitable host cells using any techniques available in the art, as described above.

Subgenomic polynucleotides of the invention can be used to propagate additional copies of the polynucleotides or to express protein, polypeptides, or fusion proteins. The subgenomic polynucleotides disclosed herein can also be used, for example, as biomarkers for tissues or chromosomes, as molecular weight markers for DNA gels, to elicit immune responses, such as the formation of antibodies against single- or double-stranded DNA, and in DNA-ligand interaction assays, to detect proteins or other molecules which interact with the nucleotide sequences.

Disease states may be associated with alterations in the expression of genes which encode proteins of the invention. Polynucleotide sequences disclosed herein can also be used to determine the involvement of any of these sequences in disease states. For example, a gene in a diseased cell can be sequenced and compared with a wild-type coding sequence of the invention. Alternatively, nucleotide probes can be constructed and used to detect normal or altered (mutant) forms of mRNA in a diseased cell. Subgenomic polynucleotides of the invention can also be used to design diagnostic tests and therapeutic compositions for diseases which may be associated with altered expression of these genes.

The present invention provides both full-length and mature forms of the disclosed proteins. Full-length forms of the proteins have the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. The full-length forms of a protein can be processed enzymatically to remove a signal sequence, resulting in a mature form of the protein. Signal sequences can be identified by examination of the amino acid sequences disclosed herein and comparison with amino acid sequences of known signal sequences (see, *e.g.*, von Heijne, 1985; Kaiser & Botstein, 1986). Similarly, transmembrane domains can be identified by examination of the amino acid sequences disclosed herein. A transmembrane domain typically contains a long stretch of 15-30 hydrophobic amino acids.

Other domains with predicted functions can also be identified. For example, the protein having the amino acid sequence shown in SEQ ID NO:23 comprises a Kunitz type serine protease inhibitor domain spanning amino acids 68 to 122 of SEQ ID NO:23. The protein having the amino acid sequence shown in SEQ ID NO:20 contains a zinc-finger motif.

Allelic variants of the disclosed subgenomic polynucleotides can occur and encode proteins which are identical, homologous, or substantially related to amino acid sequences disclosed herein (see below).

Allelic variants of subgenomic polynucleotides of the invention can be identified by hybridization of putative allelic variants with nucleotide sequences disclosed herein under stringent conditions. For example, by using the following wash conditions--2 x SCC, 0.1% SDS, room temperature twice, 30 minutes each; then 2 x SCC, 0.1% SDS, 50 °C. once, 30 minutes; then 2 x SCC, room temperature twice, 10 minutes each--allelic variants can be identified which contain at most about 25-30% basepair mismatches. More preferably, allelic variants contain 15-25% basepair mismatches, even more preferably 5-15% basepair mismatches.

Protein variants of secreted proteins of the invention are also included. Amino acids which are not involved in regions which determine biological activity can be deleted or modified without affecting biological function. Preferably, protein

variants of the invention have amino acid sequences which are at least 85%, 90%, or 95% identical to the amino acid sequences disclosed herein and have similar biological properties (see below). More preferably, the molecules are 98% identical. Modifications of interest in the protein sequences can include the alteration, substitution, replacement, insertion or deletion of a selected amino acid residue. Proteins or derivatives can be either glycosylated or unglycosylated. Techniques for making such modifications are well known to those skilled in the art (see, e.g., U.S. 4,518,584). Alternatively, variants of proteins disclosed herein can be constructed using techniques of synthetic chemistry or using recombinant DNA methods.

Preferably, amino acid changes in variants or derivatives of proteins of the invention are conservative amino acid changes, *i.e.*, substitutions of similarly charged or uncharged amino acids. A conservative amino acid change involves substitution of one amino acid for another amino acid of a family of amino acids which are structurally related in their side chains. Naturally occurring amino acids are generally divided into four families: acidic (aspartate, glutamate), basic (lysine, arginine, histidine), non-polar (alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), and uncharged polar (glycine, asparagine, glutamine, cystine, serine, threonine, tyrosine) amino acids. Phenylalanine, tryptophan, and tyrosine are sometimes classified as aromatic amino acids. It is reasonable to expect that an isolated replacement of a leucine with an isoleucine or valine, an aspartate with a glutamate, a threonine with a serine, or a similar replacement of an amino acid with a structurally related amino acid will not have a major effect on the binding properties of the resulting molecule, especially if the replacement does not involve an amino acid at a binding site involved in an interaction of the protein. Non-naturally occurring amino acids can also be used to form protein variants of the invention.

Whether an amino acid change results in a functional protein or polypeptide can readily be determined by assaying biological properties of the disclosed proteins or polypeptides, as described below. Species homologs of human subgenomic polynucleotides and proteins of the invention can also be identified by making

suitable probes or primers and screening cDNA expression libraries from other species, such as mice, monkeys, yeast, or bacteria.

5 In the case of proteins which are membrane-bound, such as cell surface receptor proteins, soluble forms of the proteins can be obtained by deleting the nucleotide sequences which encode part or all of the intracellular and transmembrane domains of the protein and expressing a fully secreted form of the protein in a host cell. Techniques for identifying intracellular and transmembrane domains, such as homology searches, can be used to identify such domains in proteins of the invention using amino acid and nucleotide sequences disclosed
10 herein.

Polypeptides consisting of less than full-length proteins of the present invention are also provided. Polypeptides of the invention can be linear or can be cyclized, for example, as described in Saragovi *et al.*, 1992, *Bio/Technology* 10, 773-778 and McDowell *et al.*, 1992, *J. Amer. Chem. Soc.* 114, 9245-9253.

15 Polypeptides can be used, for example, as immunogens, diagnostic aids, or therapeutics, and to create fusion proteins, as described below.

Polypeptide molecules consisting of less than the entire amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38 are also provided. Such polypeptides comprise at least 6,
20 8, 10, 12, 15, 18, or 20 contiguous amino acids of an amino acid sequence shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. Polypeptide molecules of the invention can also possess minor amino acid alterations which do not substantially affect the ability of the polypeptides to interact with specific molecules, such as antibodies.

25 Derivatives of the polypeptides, such as glycosylated forms, aggregative conjugates with other molecules, and covalent conjugates with unrelated chemical moieties, are also provided. Derivatives also include allelic variants, species variants, and muteins. Covalent derivatives are prepared by linkage of functionalities to groups which are found in the amino acid chain or at the N- or C-
30 terminal residue by means known in the art. Truncations or deletions of regions which do not affect biological function are also encompassed. Truncated or deleted

polypeptides can be prepared synthetically or recombinantly, or by proteolytic digestion of purified or partially purified secreted proteins of the invention.

5 Fusion proteins comprising at least 6, 8, 10, 12, 15, 18, or 20 contiguous amino acids of the disclosed proteins can also be constructed. Human fusion proteins are useful, *inter alia*, for generating antibodies against amino acid sequences and for use in various assay systems. For example, fusion proteins can be used to identify proteins which interact with secreted proteins of the invention and influence their function. Physical methods, such as protein affinity chromatography, or library-based assays for protein-protein interactions, such as the
10 yeast two-hybrid or phage display systems, can be used for this purpose. Such methods are well known in the art and can also be used as drug screens. Fusion proteins can also be used to target molecules to a specific location in a cell or to cause a molecule to be secreted or to be anchored in a cellular membrane.

15 Fusion proteins of the invention comprise two protein segments which are fused together with a peptide bond. The first protein segment comprises at least 6, 8, 10, 12, 15, 18, or 20 contiguous amino acids selected from an amino acid sequence shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38. The first protein segment can also be a full-length protein (comprising a signal sequence) or a mature protein (lacking a signal
20 sequence). The second protein segment can be a full-length protein or a protein fragment. The second protein or protein fragment can be labeled with a detectable marker, such as a radioactive, chemiluminescent, biotinylated, or fluorescent tag, or can be an enzyme which will generate a detectable product. Enzymes suitable for this purpose, such as β -galactosidase, are well known in the art.

25 Techniques for making fusion proteins, either recombinantly or by covalently linking two protein segments, are well known in the art. Fusion proteins comprising amino acid sequences of the invention can also be constructed, for example, using standard recombinant DNA methods to make a DNA construct which comprises contiguous nucleotides selected from SEQ ID NOs:1, 2, 3, 4, 5, 6,
30 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 and encoding the desired amino

acids in proper reading frame with nucleotides encoding the second protein segment.

Proteins or polypeptides of the invention can be purified free from other components with which they are normally associated in a cell, such as carbohydrates, lipids, subcellular organelles, or other proteins. An isolated protein or polypeptide is at least 90% pure. Preferably, the preparations are 95% or 99% pure. The purity of a preparation can be assessed, for example, by examining electrophoretograms of protein or polypeptide preparations at several pH values and at several polyacrylamide concentrations, as is known in the art.

Standard biochemical methods can be used to isolate proteins of the invention from tissues which express the proteins or to isolate proteins, polypeptides, or fusion proteins from recombinant host cells into which a DNA construct has been introduced. Methods of protein purification, such as size exclusion chromatography, ammonium sulfate fractionation, ion exchange chromatography, affinity chromatography, crystallization, electrofocusing, or preparative gel electrophoresis, are well known and widely used in the art.

Alternatively, proteins, fusion proteins, or polypeptides of the invention can be produced by recombinant DNA methods or by synthetic chemical methods. Synthetic chemistry methods, such as solid phase peptide synthesis, can be used to synthesize proteins, fusion proteins, or polypeptides. For production of recombinant proteins, fusion proteins, or polypeptides, coding sequences selected from the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 can be expressed in prokaryotic or eukaryotic host cells using expression systems known in the art. These expression systems include bacterial, yeast, insect, and mammalian cells (see below).

The resulting expressed protein can then be purified from the culture medium or from extracts of the cultured cells using purification procedures known in the art. For example, for proteins fully secreted into the culture medium, cell-free medium can be diluted with sodium acetate and contacted with a cation exchange resin, followed by hydrophobic interaction chromatography. Using this method, the desired protein, fusion protein, or polypeptide is typically greater than 95% pure.

Further purification can be undertaken, using, for example, any of the techniques listed above. Proteins, fusion proteins, or polypeptides can also be tagged with an epitope, such as a "Flag" epitope (Kodak), and purified using an antibody which specifically binds to that epitope.

5 It may be necessary to modify a protein produced in yeast or bacteria, for example by phosphorylation or glycosylation of the appropriate sites, in order to obtain a functional protein. Such covalent attachments can be made using known chemical or enzymatic methods.

10 Proteins or polypeptides of the invention can also be expressed in cultured cells in a form which will facilitate purification. For example, a secreted protein or polypeptide can be expressed as a fusion protein comprising, for example, maltose binding protein, glutathione-S-transferase, or thioredoxin, and purified using a commercially available kit. Kits for expression and purification of such fusion proteins are available from companies such as New England BioLabs, Pharmacia, and Invitrogen.

15 The coding sequences disclosed herein can also be used to construct transgenic animals, such as cows, goats, pigs, or sheep. Female transgenic animals can then produce proteins, polypeptides, or fusion proteins of the invention in their milk. Methods for constructing such animals are known and widely used in the art.

20 Isolated proteins, polypeptides, or fusion proteins of the invention can be used to obtain a preparation of antibodies which specifically bind to epitopes comprising amino acid sequences of the invention. Antibodies of the invention can be used, for example, to detect proteins, polypeptides, or fusion proteins of the invention which are secreted into culture medium or to identify tissues or cells which express these molecules. The antibodies can be polyclonal or monoclonal or can be single chain antibodies. Techniques for raising polyclonal and monoclonal antibodies and for constructing single chain antibodies are well known in the art.

25
30 Antibodies of the invention bind specifically to epitopes comprising amino acid sequences of the invention, preferably to epitopes not present on other proteins. Typically a minimum number of contiguous amino acids to encode an epitope is 6, 8, or 10. However, more amino acids can be part of an epitope, for

example, at least 15, 25, or 50, especially to form epitopes which involve non-contiguous residues. Specific binding antibodies do not detect other proteins on Western blots of proteins or in immunocytochemical assays. Specific binding antibodies provide a signal at least ten-fold lower than the signal provided with epitopes which do not comprise amino acid sequences of the invention. Antibodies which bind specifically to secreted proteins of the invention include those that bind to mature or full-length proteins, to polypeptides or degradation products, to fusion proteins, or to protein variants. In a preferred embodiment of the invention, the antibodies immunoprecipitate the desired protein, fusion protein, or polypeptide from solution and react with the protein, fusion protein, or polypeptide on Western blots of polyacrylamide gels.

Techniques for purifying antibodies are those which are available in the art. In a preferred embodiment, antibodies are affinity purified by passing the antibodies over a column to which amino acid sequences of the invention are bound. The bound antibody is then eluted, for example using a buffer with a high salt concentration. Any such technique may be chosen to purify antibodies of the invention.

The invention also provides DNA constructs, for expressing all or a portion of a protein of the invention in a host cell. The DNA construct comprises a promoter which is functional in the particular host cell selected. The skilled artisan can readily select an appropriate promoter from the large number of cell type-specific promoters known and used in the art. The DNA construct can also contain a transcription terminator which is functional in the host cell.

The expression construct comprises a polynucleotide segment which encodes all or a portion of a human protein encoded by SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 or a variant thereof. The polynucleotide segment is located downstream from the promoter. Transcription of the polynucleotide segment initiates at the promoter. DNA constructs can be linear or circular and can contain sequences, if desired, for autonomous replication.

The host cell comprising the DNA construct can be any suitable prokaryotic or eukaryotic cell. Expression systems in bacteria include those described in Chang

et al., *Nature* (1978) 275: 615; Goeddel *et al.*, *Nature* (1979) 281: 544; Goeddel *et al.*, *Nucleic Acids Res.* (1980) 8: 4057; EP 36,776; U.S. 4,551,433; deBoer *et al.*, *Proc. Natl. Acad. Sci. USA* (1983) 80: 21-25; and Siebenlist *et al.*, *Cell* (1980) 20: 269.

5 Expression systems in yeast include those described in Hinnen *et al.*, *Proc. Natl. Acad. Sci. USA* (1978) 75: 1929; Ito *et al.*, *J. Bacteriol.* (1983) 153: 163; Kurtz *et al.*, *Mol. Cell. Biol.* (1986) 6: 142; Kunze *et al.*, *J. Basic Microbiol.* (1985) 25: 141; Gleeson *et al.*, *J. Gen. Microbiol.* (1986) 132: 3459, Roggenkamp *et al.*, *Mol. Gen. Genet.* (1986) 202 :302); Das *et al.*, *J. Bacteriol.* (1984) 158: 1165; De Louvencourt *et al.*, *J. Bacteriol.* (1983) 154: 737, Van den Berg *et al.*, *Bio/Technology* (1990) 8: 135; Kunze *et al.*, *J. Basic Microbiol.* (1985) 25: 141; Cregg *et al.*, *Mol. Cell. Biol.* (1985) 5: 3376; U.S. 4,837,148; U.S. 4,929,555; Beach and Nurse, *Nature* (1981) 300: 706; Davidow *et al.*, *Curr. Genet.* (1985) 10: 380; Gaillardin *et al.*, *Curr. Genet.* (1985) 10: 49; Ballance *et al.*, *Biochem. Biophys. Res. Commun.* (1983) 112: 284-289; Tilburn *et al.*, *Gene* (1983) 26: 205-22,, Yelton *et al.*, *Proc. Natl. Acad. Sci. USA* (1984) 81: 1470-1474; Kelly and Hynes, *EMBO J.* (1985) 4: 475479; EP 244,234; and WO 91/00357.

15 Expression of heterologous genes in insects can be accomplished as described in U.S. 4,745,051; Friesen *et al.* (1986) "The Regulation of Baculovirus Gene Expression" in: THE MOLECULAR BIOLOGY OF BACULOVIRUSES (W. Doerfler, ed.); EP 127,839; EP 155,476; Vlak *et al.*, *J. Gen. Virol.* (1988) 69: 765-776; Miller *et al.*, *Ann. Rev. Microbiol.* (1988) 42: 177; Carbonell *et al.*, *Gene* (1988) 73: 409; Maeda *et al.*, *Nature* (1985) 315: 592-594; Lebacq-Verheyden *et al.*, *Mol. Cell. Biol.* (1988) 8: 3129; Smith *et al.*, *Proc. Natl. Acad. Sci. USA* (1985) 82: 8404; Miyajima *et al.*, *Gene* (1987) 58: 273; and Martin *et al.*, *DNA* (1988) 7:99. Numerous baculoviral strains and variants and corresponding permissive insect host cells from hosts are described in Luckow *et al.*, *Bio/Technology* (1988) 6: 47-55, Miller *et al.*, in GENERIC ENGINEERING (Setlow, J.K. *et al.* eds.), Vol. 8 (Plenum Publishing, 1986), pp. 277-279; and Maeda *et al.*, *Nature*, (1985) 315: 592-594.

25 Mammalian expression can be accomplished as described in Dijkema *et al.*,

EMBO J. (1985) 4: 761; Gorman *et al.*, *Proc. Natl. Acad. Sci. USA* (1982b) 79: 6777; Boshart *et al.*, *Cell* (1985) 41: 521; and U.S. 4,399,216. Other features of mammalian expression can be facilitated as described in Ham and Wallace, *Meth. Enz.* (1979) 58: 44; Barnes and Sato, *Anal. Biochem.* (1980) 102: 255; U.S. 4,767,704; U.S. 4,657,866; U.S. 4,927,762; U.S. 4,560,655; WO 90/103430, WO 87/00195, and U.S. RE 30,985.

DNA constructs of the invention can be introduced into host cells using any technique known in the art. These techniques include transferrin-polycation-mediated DNA transfer, transfection with naked or encapsulated nucleic acids, liposome-mediated cellular fusion, intracellular transportation of DNA-coated latex beads, protoplast fusion, viral infection, electroporation, and calcium phosphate-mediated transfection.

Alternatively, expression of an endogenous gene encoding a protein of the invention can be manipulated by introducing by homologous recombination a DNA construct comprising a transcription unit in frame with the endogenous gene, to form a homologously recombinant cell comprising the transcription unit. The transcription unit comprises a targeting sequence, a regulatory sequence, an exon, and an unpaired splice donor site. The new transcription unit can be used to turn the endogenous gene on or off as desired. This method of affecting endogenous gene expression is taught in U.S. 5,641,670, which is incorporated herein by reference.

The targeting sequence is a segment of at least 10, 12, 15, 20, or 50 contiguous nucleotides selected from the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19. The transcription unit is located upstream to a coding sequence of the endogenous gene. The exogenous regulatory sequence directs transcription of the coding sequence of the endogenous gene.

Secreted proteins of the invention have a variety of uses. For example, secreted proteins can be used in assays to determine biological activities, such as cytokine, cell proliferation, or cellular differentiation activities, tissue growth or

regeneration, activin or inhibin activity, chemotactic or chemokinetic activity, hemostatic or thrombolytic activity, receptor/ligand activity, tumor inhibition, or anti-inflammatory activity. Assays for these activities are known in the art and are disclosed, for example, in U.S. 5,654,173, which is incorporated herein by reference.

Proteins of the invention can also be used as biomarkers, to identify tissues or cell types which express the proteins, or a stage- or disease-specific alteration in protein expression. Proteins of the invention can be used in protein interaction assays, to identify ligands or binding proteins. Compounds which affect the biological activities of the secreted proteins or their ability to interact with specific ligands can be identified using proteins of the invention in screening assays. Proteins and antibodies of the invention can also be used to design diagnostic tests and therapeutic compositions for diseases which may be associated with altered expression of these proteins. Fusion proteins comprising, for example, signal sequences or transmembrane domains of the disclosed proteins, can be used to target other protein domains to cellular locations in which the domains are not normally found, such as bound to a cellular membrane or secreted extracellularly.

Further objects, features, and advantages of the present invention will readily occur to the skilled artisan provided with the disclosure above.

SYNOPSIS OF THE INVENTION

1. An isolated and purified human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

2. An isolated and purified human protein having an amino acid sequence which is at least 85% identical to an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

3. The isolated and purified human protein of item 2 wherein the amino acid sequence is at least 90% identical.

4. The isolated and purified human protein of item 2 wherein the amino acid sequence is at least 95% identical.

5 5. The isolated and purified human protein of item 2 wherein the amino acid sequence is at least 98% identical.

6. An isolated and purified human polypeptide comprising at least 6 contiguous amino acids of an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24,
10 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

7. A fusion protein comprising a first protein segment and a second protein segment fused together by means of a peptide bond, wherein the first protein segment consists of at least 6 contiguous amino acids selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23,
15 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

8. A preparation of antibodies which specifically bind to the human protein of item 1.

9. The preparation of antibodies of item 8 wherein the antibodies are monoclonal.

20 10. The preparation of antibodies of item 8 wherein the antibodies are polyclonal.

11. The preparation of antibodies of item 8 wherein the antibodies are single chain antibodies.

12. An isolated and purified subgenomic polynucleotide having a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18,
25 and 19.

13. An isolated and purified subgenomic polynucleotide consisting of at least 10 contiguous nucleotides of a nucleotide sequence selected from the group

consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

14. An isolated gene corresponding to a cDNA sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

15. A DNA construct for expressing all or a portion of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, comprising:

a promoter; and

a polynucleotide segment encoding at least 6 contiguous amino acids of the human protein, wherein the polynucleotide segment is located downstream from the promoter, wherein transcription of the polynucleotide segment initiates at or 3' to the promoter.

16. A host cell comprising a DNA construct comprising:

a promoter; and

a polynucleotide segment encoding at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, wherein the polynucleotide segment is located downstream from the promoter and wherein transcription of the polynucleotide segment initiates at or 3' to the promoter.

17. A homologously recombinant cell having incorporated therein a new transcription initiation unit, wherein the new transcription initiation unit comprises in 5' to 3' order:

(a) an exogenous regulatory sequence;

(b) an exogenous exon; and

(c) a splice donor site,

wherein the transcription initiation unit is located upstream to a coding sequence of a gene, wherein the gene comprises a nucleotide sequence selected from the group

consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19, and wherein the exogenous regulatory sequence controls transcription of the coding sequence of the gene.

18. A method of producing a human protein, comprising the steps of:

5

growing a culture of a cell comprising a DNA construct comprising

(1) a promoter and (2) a polynucleotide segment encoding at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, wherein the polynucleotide segment is located downstream from the promoter and wherein transcription of the polynucleotide segment initiates at or 3' to the promoter; and;

10

purifying the protein from the culture.

19. A method of producing a human protein, comprising the steps of:

15

growing a culture of a homologously recombinant cell having incorporated therein a new transcription initiation unit, wherein the new transcription initiation unit comprises in 5' to 3' order:

(a) an exogenous regulatory sequence;

(b) an exogenous exon; and

(c) a splice donor site,

20

wherein the transcription initiation unit is located upstream to a coding sequence of a gene, wherein the gene comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 and wherein the exogenous regulatory sequence controls transcription of the coding sequence of the gene; and

25

purifying the protein from the culture.

20. A method of identifying a secreted polypeptide which is modified by rough microsomes, comprising the steps of:

transcribing *in vitro* a population of cDNA molecules whereby a population of cRNA molecules is formed;

translating a first portion of the population of cRNA molecules *in vitro* in the absence of rough microsomes whereby a first population of polypeptides is formed;

5 translating a second portion of the population of cRNA molecules *in vitro* in the presence of rough microsomes whereby a second population of polypeptides is formed;

comparing the first population of polypeptides with the second population of polypeptides; and

10 detecting polypeptide members of the second population which have been modified by the rough microsomes.

21. The method of item 20 wherein the population of cDNA molecules is synthesized by reverse transcription of a population of mRNA molecules.

22. The method of item 21 wherein the mRNA molecules are isolated from a mammal.

15 23. The method of item 22 wherein the mRNA molecules are isolated from a human.

24. The method of item 20 wherein the population of cDNA molecules is obtained from a cDNA library.

20 25. The method of item 24 wherein the cDNA library is derived from a mammalian genome.

26. The method of item 25 wherein the cDNA library is derived from a human genome.

SEQUENCE LISTING

(1) GENERAL INFORMATION

- (i) APPLICANT: Chiron Corporation
- (ii) TITLE OF THE INVENTION: Secreted Human Proteins
- (iii) NUMBER OF SEQUENCES: 38
- (iv) CORRESPONDENCE ADDRESS:
 - (A) ADDRESSEE: Banner & Witcoff
 - (B) STREET: 1001 G Street, NW
 - (C) CITY: Washington
 - (D) STATE: DC
 - (E) COUNTRY: USA
 - (F) ZIP: 20001
- (v) COMPUTER READABLE FORM:
 - (A) MEDIUM TYPE: Diskette
 - (B) COMPUTER: IBM Compatible
 - (C) OPERATING SYSTEM: DOS
 - (D) SOFTWARE: FastSEQ for Windows Version 2.0
- (vi) CURRENT APPLICATION DATA:
 - (A) APPLICATION NUMBER:
 - (B) FILING DATE: 11-DEC-1997

(C) CLASSIFICATION:

(vii) PRIOR APPLICATION DATA:

(A) APPLICATION NUMBER: 60/032757

(B) FILING DATE: 11-DEC-1996

(viii) ATTORNEY/AGENT INFORMATION:

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(B) REGISTRATION NUMBER: 32141

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2441.39505;1369.002;1452.001

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(C) TELEX:

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 2063 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ix) FEATURE:

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

GAATTCGGCA CGAGGCCTCA GTCTTCCAGG GCGGCGGTGG GTGTCCGCTT CTCTCTGCTC	60
TTCGACTGCA CCGCACTCGC GCGTGACCCT GACTCCCCCT AGTCAGCTCA GCGGTGCTGC	120
CATGGCGTGG CGGCGGCGCG AAGCCGGCGT CGGGGCTCGC GCGGTGTTGG CTCTGGCGTT	180
GCTCGCCCTG GCCCTGTGCG TGCCCGGGGC CCGGGGCCGG GCTCTCGAGT GGTTCGCGC	240

CGTGGTAAAC ATCGAGTACG TGGACCCGCA GACCAACCTG ACGGTGTGGA GCGTCTCGGA	300
GAGTGGCCGC TTCGGCGACA GCTCGCCCAA GGAGGGCGCG CATGGCCTGG TGGGCGTCCC	360
GTGGGCGCCC GCGGAGACC TCGAGGGCTG CGCGCCCGAC ACGCGCTTCT TCGTGCCCGA	420
CCCCGGCGGC CGAGGGGCGG CGCCCTGGGT CGCCCTGGTG GCTCGTGGGG GCTGCACCTT	480
CAAGGACAAAG GTGCTGGTGG CGGCGCGGAG GAACGCCTCG GCCGTGCTCC TCTACAATGA	540
GGAGCGCTAC GGGAACATCA CCTTGCCCAT GTCTCACGCG GGAACAGGAA ATATAGTGGT	600
CATTATGATT AGCTATCCAA AAGGAAGAGA AATTTTGGAG CTGGTGCAA AAGGAATTCC	660
AGTAACGATG ACCATAGGGG TTGGCACCCG GCATGTACAG GAGTTCATCA GCGGTCAGTC	720
TGTGGTGTTT GTGGCCATTG CCTTCATCAC CATGATGATT ATCTCGTTAG CCTGGCTAAT	780
ATTTTACTAT ATACAGCGTT TCCTATATAC TGGCTCTCAG ATTGGAAGTC AGAGCCATAG	840
AAAAGAACT AAGAAAGTTA TTGGCCAGCT TCTACTTCAT ACTGTAAAGC ATGGAGAAAA	900
GGGAATTGAT GTTGATGCTG AAAATTGTGC AGTGTGTATT GAAAATTTCA AAGTAAAGGA	960
TATTATTAGA ATTCTGCCAT GCAAGCATAT TTTTCATAGA ATATGCATTG ACCCATGGCT	1020
TTTGATCAC CGAACATGTC CAATGTGTAA ACTTGATGTC ATCAAAGCCC TAGGATATTG	1080
GGGAGAGCCT GGGGATGTAC AGGAGATGCC TGCTCCAGAA TCTCCTCCTG GAAGGGATCC	1140
AGCTGCAAAT TTGAGTCTAG CTTTACCAGA TGATGACGGA AGTGATGACA GCAGTCCACC	1200
ATCAGCCTCC CCTGCTGAAT CTGAGCCACA GTGTGATCCC AGCTTTAAAG GAGATGCAGG	1260
AGAAAATACG GCATTGCTAG AAGCCGGCAG GAGTGACTCT CGGCATGGAG GACCCATCTC	1320
CTAGCACACG TGCCCACTGA AGTGGCACCA ACAGAAGTTT GGCTTGAAC AAAGGACATT	1380
TTATTTTTTT TACTTTAGCA CATAATTTGT ATATTTGAAA ATAATGTATA TTATTTTACC	1440
TATTAGATTC TGATTGATA TACAAAGGAC TAAGATATTT TCTTCTTGAA GAGACTTTTC	1500
GATTAGTCCT CATATATTTA TCTACTAAAA TAGAGTGTTT ACCATGAACA GTGTGTTGCT	1560
TCAGACTATT ACAAAGACAA CTGGGGCAGG TACTCTAATA TAAAGGACAG GTGGTGTTTC	1620
TAAATAATTG GCTGCTATGG TTCTGTAAAA ACCAGTTAAT TCTATTTTTC AAGGTTTTTG	1680
GCAAAGCACA TCAATGTTAG ACTAGTTGAA GTGGAATTGT ATAATTCAAT TCGATAATTG	1740
ATCTCATGGG CTTTCCCTGG AGGAAAGGTT TTTTTTGTTG TTTTTTTTTT AAGAACTGA	1800
AACTTGTAAG CTGAGATGTC TGTAGCTTTT TTGCCCATCT GTAGTGATG TGAAGATTTT	1860
AAAACCTGAG AGCACTTTTT CTTTGTTTAG AATTATGAGA AAGGCACTAG ATGACTTTAG	1920
GATTGTCATT TTTCCCTTTA TTGCCTCATT TCTGTGACG CCTTGTTGGG GAGGGAAATC	1980
TGTTTATTTT TTCCTACAAA TAAAAAGCTA AGATTCTATA TCGCAAAAAA AAAAAAAAAA	2040
AAAAAAAAA TTCCTGCGGC CGC	2063

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1328 base pairs

- (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

GAATTCGGCA CGAGGTAGGC AAGGGATAAA AAGGCACCTA AGGCCCTTTT GCAATAAGAA	60
GCCAGATGGA TAAAGGAAGT GCTGGTCACC CTGGAGGTGT ACTGGTTTGG GGAAGGTCCC	120
CGGCCCCCAG AGCCCTCTGG GGAGCCTCAC CCTGGCTCTC CCCACTCACC TCAGCCCTCA	180
GGCAGCCCCCT CCACAGGGCC CCTCTCCTGC CTGGACAGCT CTGCTGGTCT CCCCCTCCCC	240
TGGAGAAGAA CAAGGCCATG GGTCGGCCCC TGCTGCTGCC CCTGCTGCTC CTGCTGCAGC	300
CGCCAGCATT TCTGCAGCCT GGTGGCTCCA CAGGATCTGG TCCAAGCTAC CTTTATGGGG	360
TCACTCAACC AAAACACCTC TCAGCCTCCA TGGGTGGCTC TGTGGAAATC CCCTTCTCCT	420
TCTATACCC CTGGGAGTTA GCCATAGTTC CCAACGTGAG AATATCCTGG AGACGGGGCC	480
ACTTCCACGG GCAGTCCTTC TACAGCACAA GGCCGCCTTC CATTACAAAG GATTATGTGA	540
ACCGGCTCTT TCTGAACTGG ACAGAGGGTC AGGAGAGCGG CTTCTCAGG ATCTCAAACC	600
TGCGGAAGGA GGACCAGTCT GTGTATTTCT GCCGAGTCGA GCTGGACACC CGGAGATCAG	660
GGAGGCAGCA GTTGCACTCC ATCAAGGGGA CCAAACTCAC CATCACCAG GCTGTCACAA	720
CCACCACCAC CTGGAGGCCC AGCAGCACAA CCACCATAGC CGGCCTCAGG GTCACAGAAA	780
GCAAAGGGCA CTCAGAAATCA TGGCACCTAA GTCTGGACAC TGCCATCAGG GTTGCACTGG	840
CTGTCGCTGT GCTCAAACT GTCATTTTGG GACTGCTGTG CCTCCTCCTC CTGTGGTGGA	900
GGAGAAGGAA AGGTAGCAGG GCGCCAAGCA GTGACTTCTG ACCAACAGAG TGTGGGGAGA	960
AGGGATGTGT ATTAGCCCCG GAGGACGTGA TGTGAGACCC GCTTGTGAGT CCTCCACACT	1020
CGTTCCCCAT TGGCAAGATA CATGGAGAGC ACCCTGAGGA CCTTTAAAAG GCAAAGCCGC	1080
AAGGCAGAAG GAGGCTGGGT CCCTGAATCA CCGACTGGAG GAGAGTTACC TACAAGAGCC	1140
TTTATCCAGG AGCATCCACA CTGCAATGAT ATAGGAATGA GGTCTGAACT CCACTGAATT	1200
AAACCACTGG CATTTGGGGG CTGTTTATTA TAGCAGTGCA AAGAGTTCCT TTATCCTCCC	1260
CAAGGATGGA AAAATACAAT TTATTTTGCT TACCATAAAA AAAAAAAAAA AAAAATTCCT	1320
GCGGCCGC	1328

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1689 base pairs
 (B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

GAATTCGGCA CGAGGGCAAG ATTCGATACA AAACCAATGA ACCTGTGTGG GAGGAAAAC	60
TCACCTTTCTT CATTACAAAT CCCAAGCGCC AGGACCTTGA AGTTGAGGTC AGAGACGAGC	120
AGCACCAGTG TTCCCTGGGG AACCTGAAGG TCCCCCTCAG CCAGCTGCTC ACCAGTGAGG	180
ACATGACTGT GAGCCAGCGC TTCCAGCTCA GTAACCTCGG TCCAAACAGC ACCATCAAGA	240
TGAAGATTGC CCTGCGGGTG CTCCATCTCG AAAAGCGAGA AAGGCCTCCA GACCACCAAC	300
ACTCAGCTCA AGTCAAACGT CCCTCTGTGT CCAAAGAGGG GAGGAAAACA TCCATCAAAT	360
CTCATATGTC TGGGTCTCCA GGCCCTGGTG GCAGCAACAC AGCTCCATCC ACACCAGTCA	420
TTGGGGGCAG TGATAAGCCT GGTATGGAAG AAAAGGCCCA GCCCCCTGAG GCCGGCCCTC	480
AGGGGCTGCA CGACCTGGGC AGAAGCTCCT CCAGCCTCCT GGCCTCCCCA GGCCACATCT	540
CAGTCAAGGA GCCGACCCCC AGCATCGCCT CGGACATCTC GCTGCCCATC GCCACCCAGG	600
AGCTGCGGCA AAGGCTGAGG CAGCTGGAAA ACGGGACGAC CCTGGGACAG TCTCCACTGG	660
GGCAGATCCA GCTGACCATC CGGCACAGCT CGCAGAGAAA CAAGCTTATC GTGGTCGTGC	720
ATGCCTGCAG AAACCTCATT GCCTTCTCTG AAGACGGCTC TGACCCCTAT GTCCGCATGT	780
ATTTATTACC AGACAAGAGG CGGTCAGGAA GGAGGAAAAC ACACGTGTCA AAGAAAACAT	840
TAAATCCAGT GTTTGATCAA AGCTTTGATT TCAGTGTTTC GTTACCAGAA GTGCAGAGGA	900
GAACGCTCGA CGTTGCCGTG AAGAACAGTG GCGGCTTCCT GTCCAAAGAC AAAGGGCTCC	960
TTGGCAAAGT ATTGGTTGCT CTGGCATCTG AAGAACTTGC CAAAGGCTGG ACCCAGTGGT	1020
ATGACCTCAC GGAAGATGGG ACGAGGCCTC AGGCGATGAC ATAGCCGCAG CAGGCAGGAG	1080
GCGTCCCTCT CAGCGTAGCT CTCCACCTCT ACCCGGAACA CACCCCTCTCA CAGACGTACC	1140
AATGTTATTT TTATAATTTT ATGGATTTAG TTATACATAC CTTAATAGTT TTATAAAATT	1200
GTTGACATTT CAGGCAAATT TGGCCAATAT TATCATTGAA TTTTCTGTGT TGGATTTCCT	1260
CTAGGATTTT GCCAGTTCCT ACAACGTGCA GTAGGGCGGC GGTAGCTCTT GTGTCTGTGG	1320
ACTCTGCTCA GCTGTGTCCG TAGGAGTCGG ATGTGTCTGT GCTTTATTAT GGCCTTGTTT	1380
ATATATCACT GAGGTATACT ATGCCATGTA AATAGACTAT TTTTATAAT CTTAACATGC	1440
TGGTTTAAAT TCAGAAGGAA ATAGATCAAG GAAATATATA TATTTTCTTC TAAAACTTAT	1500
TAAATTCGTG TGACAAATAA TCATTTTCAT CTTGGCAGCA AAAAGTTCTC AGTGACCTAT	1560
TTTGTGGTGT TTCTTTTGA AAAGAAAAGC TGAAATATTA TTAAATGCTA GTATGTTTCT	1620
GCCCATTATG AAAGATGAAA TAAAGTATTC AAAATATTAA AAAAAAAAAA AAAAAATTCC	1680
TGCGGCCCGC	1689

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1505 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

GAATTCGGCA CGAGGAGCAG ATCTGCAAGA GTTTCGTTTA TGGAGGCTGC TTGGGCAACA	60
AGAACAACATA CCTTCGGGAA GAAGAGTGCA TTCTAGCCTG TCGGGGTGTG CAAGGTGGGC	120
CTTTGAGAGG CAGCTCTGGG GCTCAGGCGA CTTTCCCCCA GGGCCCCTCC ATGGAAGGC	180
GCCATCCAGT GTGCTCTGGC ACCTGTCAGC CCACCCAGTT CCGCTGCAGC AATGGCTGCT	240
GCATCGACAG TTTCTGGAG TGTGACGACA CCCCCAACTG CCCCAGCGCC TCCGACGAGG	300
CTGCCTGTGA AAAATACACG AGTGGCTTTG ACGAGCTCCA GCGCATCCAT TTCCCCAGCG	360
ACAAAGGGCA CTGCGTGGAC CTGCCAGACA CAGGACTCTG CAAGGAGAGC ATCCCGCGCT	420
GGTACTACAA CCCCTTCAGC GAACACTGCG CCCGCTTTAC CTATGGTGGT TGTTACGGCA	480
ACAAGAACAA CTTTGAGGAA GAGCAGCAGT GCCTCGAGTC TTGTCGCGGC ATCTCCAAGA	540
AGGATGTGTT TGGCCTGAGG CGGGAAATCC CCATTCCCAG CACAGGCTCT GTGGAGATGG	600
CTGTGCGAGT GTTCTGGTC ATCTGCATTG TGGTGGTGGT AGCCATCTTG GGTACTGCT	660
TCTTCAAGAA CCAGAGAAAG GACTTCCACG GACACCACCA CCACCACCA CCCACCCCTG	720
CCAGCTCCAC TGTCTCCACT ACCGAGGACA CGGAGCACCT GGTCTATAAC CACACCACGC	780
GGCCCCTCTG AGCCTGGGTC TCACCGGCTC TCACCTGGCC CTGCTTCCTG CTTGCCAAGG	840
CAGAGGCCTG GGCTGGGAAA AACTTTGGAA CCAGACTCTT GCCTGTTTCC CAGGCCCCACT	900
GTGCCTCAGA GACCAGGGCT CCAGCCCCTC TTGGAGAAGT CTCAGCTAAG CTCACGTCCT	960
GAGAAAGCTC AAAGGTTTGG AAGGAGCAGA AAACCCTTGG GCCAGAAGTA CCAGACTAGA	1020
TGGACCTGCC TGCATAGGAG TTTGGAGGAA GTTGGAGTTT TGTTTCCTCT GTTCAAAGCT	1080
GCCTGTCCCT ACCCATGGT GCTAGGAAGA GGAGTGGGGT GGTGTCAGAC CCTGGAGGCC	1140
CCAACCCTGT CCTCCGAGC TCCTCTTCCA TGCTGTGCGC CCAGGGCTGG GAGGAAGGAC	1200
TTCCCTGTGT AGTTTGTGCT GTAAAGAGTT GCTTTTGTGTT TATTTAATGC TGTGGCATGG	1260
GTGAAGAGGA GGGGAAGAGG CCTGTTTGGC CTCTCTATCC TCTCTTCTC TTCCCCAAG	1320
ATTGAGCTCT CTGCCCTTGA TCAGCCCCAC CCTGGCCTAG ACCAGCAGAC AGAGCCAGGA	1380
GAAGCTCAGC TGCATTCCGC AGCCCCACC CCCAAGGTTT TCCAACATCA CAGCCCAGCC	1440
CGCCCACTGG GTAATAAAAG TGGTTTGTGG AAAAAAAAAA AAAAAAAAAA AAGTCCTGCG	1500

GCCGC

1505

(2) INFORMATION FOR SEQ ID NO:5:

(1) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 2002 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

GAATTCGGCA	CGAGGGCCAT	GGCCGGGCTA	TCCCGCGGGT	CCGCGCGCGC	ACTGCTCGCC	60
GCCCTGCTGG	CGTCGACGCT	GTTGGCGCTG	CTCGTGTCGC	CCGCGCGGGG	TCGCGGCGGC	120
CGGGACCACG	GGGACTGGGA	CGAGGCCTCC	CGGCTGCCGC	CGCTACCACC	CCGCGAGGAC	180
GCGGCGCGCG	TGGCCCCTT	CGTGACGCAC	GTCTCCGACT	GGGGCGCTCT	GGCCACCATC	240
TCCACGCTGG	AGGCGGTGCG	CGGCCGGCCC	TTGCGCGACG	TCCTCTCGCT	CAGCGACGGG	300
CCCCCGGGCG	CGGGCAGCGG	CGTGCCCTAT	TTCTACCTGA	GCCCGCTGCA	GCTCTCCGTG	360
AGCAACCTGC	AGGAGAATCC	ATATGCTACA	CTGACCATGA	CTTTGGCACA	GACCAACTTC	420
TGCAAGAAAC	ATGGATTGTA	TCCACAAAGT	CCCCTTTGTG	TTACATAAT	GCTGTCAGGA	480
ACTGTGACCA	AGGTGAATGA	AACAGAAATG	GATATTGCAA	AGCATTCTGT	ATTCATTCTG	540
CACCCTGAGA	TGAAAACCTG	GCCTTCCAGC	CATAATTGGT	TCTTTGCTAA	GTTGAATATA	600
ACCAATATCT	GGGTCTCTGA	CTACTTTGGT	GGACCAAAAA	TCGTGACACC	AGAAGAATAT	660
TATAATGTCA	CAGTTCAGTG	AAGCAGACTG	TGGTGAATTT	AGCAACACTT	ATGAAGTTTC	720
TTAAAGTGGC	TCATACACAC	TTAAAAGGCT	TAATGTTTCT	CTGGAAAGCG	TCCCAGAATA	780
TTAGCCAGTT	TTCTGTCACA	TGCTGGTTTG	TTTGCTTGCT	TGTTTACTTG	CTTGTTTACC	840
AATAGAGTTG	ACCTGTTATT	GGATTTCCTG	GAAGATGTGG	TAGCTACTTT	TTTCCTATTT	900
TGAAGCCATT	TTCTAGAGAG	AATATCCTTC	ACTATAATCA	AATAAGTTTT	GTCCCATCAA	960
TTCCAAAGAT	GTTTCCAGTG	GTGCTCTTGA	AGAGGAATGA	GTACCAGTTT	TAAATTGCCC	1020
ATTGGCATT	GAAGGTAGTT	GAGTATGTGT	TCTTTATTCC	TAGAAGCCAC	TGTGCTTGGT	1080
AGAGTGCAATC	ACTCACCACA	GCTGCCTCTT	GAGCTGCCTG	AGCCTGGTGC	AAAAGGATTG	1140
GCCCCCATTA	TGGTGCTTCT	GAATAAATCT	TGCCAAGATA	GACAAACAAT	GATGAAACTC	1200
AGATGGAGCT	TCCTACTCAT	GTTGATTTAT	GTCTCACAAT	CCTGGGTATT	GTTAATTCAA	1260
CATAGGGTGA	AACTATTTCT	GATAAAGAAC	TTTTGAAAAA	CTTTTATAC	TCTAAAGTGA	1320
TACTCAGAAC	AAAAGAAAGT	CATAAACTC	CTGAATTTAA	TTTCCCCACC	TAAGTCGAGA	1380

CAGTATTATC AAAACACATG TGCACACAGA TTATTTTTTG GCTCCAAAAC TGGATTGCAA	1440
AAGAAAGAGG AGAGATATTT TGTGTGTTCC TGGTATTCTT TTATAAGTAA AGTTACCCAG	1500
GCATGGACCA GCTTCAGCCA GGGACAAAAT CCCCTCCCAA ACCACTCTCC ACAGCTTTTT	1560
AAAAATACTT CTA CTCTTAA CAATTACCTA AGGTTCTTTC AAACCCCCC AACTCTTAAT	1620
AGCTTCTAGT GCTGCTACAA TCTAAGTCAG GTCACCAGAG GGAAGAGAAC ATGGCATTAA	1680
AAGAATCACA TCTTCAGAAG AGAAGACACT AATATTATTA CCCATATACA TGATTTCAGA	1740
AGATGACATA AGATTCTCT TAAAGAGGAA ATGTCAGGAA TCAAGCCACT GAATCCTTAA	1800
AGAGAAAAGT TGAATATGAG TCATTGTGTC TGAAAAGTGC AAAGTGAAGT TAACTGAGAT	1860
CCAGCAAACA GGTTCCTGTTT AAGAAAAATA ATTTATACTA AATTTAGTAA AATGGACTTC	1920
TTATTCAAAG CATCAATAAT TAAAGAATT ATTTTAAAAA AAAAAAAAAA AAAAAAAAAA	1980
AAAAAAAAAT TCCTGCGGCC GC	2002

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1322 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

GAATTCGGCA CGAGGGCCAC GACTCTGCTG GCATTTCTTC TATAGCCACT GGAATCTGAT	60
CCTGATTGTC TTCCACTACT ACCAGGCCAT CACCACTCCG CCTGGGTACC CACCCCAGGG	120
CAGGAATGAT ATCGCCACCG TCTCCATCTG TAAGAAGTGC ATTTACCCCA AGCCAGCCCCG	180
AACACACCAC TGCAGCATCT GCAACAGGTG TGTGCTGAAG ATGGATCACC ACTGCCCCTG	240
GCTAAACAAT TGTGTGGGCC ACTATAACCA TCGGTACTTC TTCTCTTTCT GCTTTTTTCAT	300
GACTCTGGGC TGTGTCTACT GCAGCTATGG AAGTTGGGAC CTTTTCGGG AGGCTTATGC	360
TGCCATTGAG AAAATGAAAC AGCTCGACAA GAACAACTA CAGGCGGTTG CCAACCAGAC	420
TTATCACCAG ACCCCACCAC CCACCTTCTC CTTTCGAGAA AGGATGACTC ACAAGAGTCT	480
TGTCTACCTC TGGTTCCTGT GCAGTTCTGT GGCATTGCC CTGGGTGCCC TAACTGTATG	540
GCATGCTGTT CTCATCAGTC GAGGTGAGAC TAGCATCGAA AGGCACATEA ACAAGAAGGA	600
GAGACGTCGG CTACAGGCCA AGGGCAGAGT ATTTAGGAAT CCTTACAACT ACGGCTGCTT	660
GGACAAGTGG AAGGTATTCC TGGGTGTGGA TACAGGAAGG CACTGGCTTA CTCGGGTGCT	720
CTTACCTTCT ACTCACTTGC CCCATGGGAA TGGAATGAGC TGGGAGCCCC CTCCCTGGGT	780

GACTGCTCAC TCAGCCTCTG TGATGGCAGT GTGAGCTGGA CTGTGTCAGC CACGACTCGA	840
GCACCTCATTC TGCTCCCTAT GTTATTTCAA GGGCCTCCAA GGGCAGCTTT TCTCAGAATC	900
CTTGATCAAA AAGAGCCAGT GGGCCTGCCT TAGGGTACCA TGCAGGACAA TTCAAGGACC	960
AGCCTTTTTTA CCACTGCAGA AGAAAGACAC AATGTGGAGA AATCTTAGGA CTGACATCCC	1020
TTTACTCAGG CAAACAGAAG TTCCAACCCC AGACTAGGGG TCAGGCAGCT AGCTACCTAC	1080
CTTGCCCAGT GCTGACCCGG ACCTCCTCCA GGATACAGCA CTGGAGTTGG CCACCACCTC	1140
TTCTACTTGC TGTCTGAAAA AACACCTGAC TAGTACAGCT GAGATCTTGG CTTCTCAACA	1200
GGGCAAAGAT ACCAGGCCTG CTGCTGAGGT CACTGCCACT TCTCACATGC TGCTTAAGGG	1260
AGCACAAATA AAGGTATTCG ATTTTAAAAA AAAAAAAAAA AAAAAAAT TCCTGCGGCC	1320
GC	1322

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1573 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

GAATTCGGCA CGAGGAGCCT GCCTTCATCT AGGATGGCTC CTCTGGGCAT GCTGCTTGGG	60
CTGCTGATGG CCGCCTGCTT CACCTTCTGC CTCAGTCATC AGAACCTGAA GGAGTTTGCC	120
CTGACCAACC CAGAGAAGAG CAGCACAAA GAAACAGAGA GAAAAGAAAC CAAAGCCGAG	180
GAGGAGCTGG ATGCCGAAGT CCTGGAGGTG TTCCACCCGA CGCATGAGTG GCAGGCCCTT	240
CAGCCAGGGC AGGCTGTCCC TGCAGGATCC CACGTACGGC TGAATCTTCA GACTGGGGAA	300
AGAGAGGCAA AACTCCAATA TGAGGACAAG TTCCGAAATA ATTTGAAAGG CAAAAGGCTG	360
GATATCAACA CCAACACCTA CACATCTCAG GATCTCAAGA GTGCACTGGC AAAATTCAAG	420
GAGGGGGCAG AGATGGAGAG TTCAAAGGAA GACAAGGCAA GGCAGGCTGA GGTAAAGCGG	480
CTCTTCCGCC CCATTGAGGA ACTGAAGAAA GACTTTGATG AGCTGAATGT TGTCATTGAG	540
ACTGACATGC AGATCATGGT ACGGCTGATC AACAAAGTTCA ATAGTTCCAG CTCCAGTTTG	600
GAAGAGAAGA TTGCTGCGCT CTTTGATCTT GAATATTATG TCCATCAGAT GGACAATGCG	660
CAGGACCTGC TTTCTTTGG TGGTCTTCAA GTGGTGATCA ATGGGCTGAA CAGCACAGAG	720
CCCCTCGTGA AGGAGTATGC TCGTTTGTG CTGGGCGCTG CCTTTTCCAG CAACCCCAAG	780
GTCCAGGTGG AGGCCATCGA AGGGGGAGCC CTGCAGAAGC TGCTGGTCAT CCTGGCCACG	840

GAGCAGCCGC	TCACTGCAAA	GAAGAAGGTC	CTGTTTGAC	TGTGCTCCCT	GCTGCGCCAC	900
TTCCCCTATG	CCCAGCGGCA	GTTCTGAAG	CTCGGGGGGC	TGCAGGTCCT	GAGGACCCTG	960
GTGCAGGAGA	AGGGCACGGA	GGTGCTCGCC	GTGCGCGTGG	TCACACTGCT	CTACGACCTG	1020
GTCACGGAGA	AGATGTTCGC	CGAGGAGGAG	GCTGAGCTGA	CCCAGGAGAT	GTCCCCAGAG	1080
AAGCTGCAGC	AGTATCGCCA	GGTACACCTC	CTGCCAGGCC	TGTGGGAACA	GGGCTGGTGC	1140
GAGATCACGG	CCCACCTCCT	GGCGCTGCCC	GAGCATGATG	CCCGTGAGAA	GGTGCTGCAG	1200
AACTGGGCG	TCCTCCTGAC	CACCTGCCGG	GACCGCTACC	GTCAGGACCC	CCAGCTCGGC	1260
AGGACACTGG	CCAGCCTGCA	GGCTGAGTAC	CAGGTGCTGG	CCAGCCTGGA	GCTGCAGGAT	1320
GGTGAGGACG	AGGGCTACTT	CCAGGAGCTG	CTGGGCTCTG	TCAACAGCTT	GCTGAAGGAG	1380
CTGAGATGAG	GCCCCACACC	AGGACTGGAC	TGGGATGCCG	CTAGTGAGGC	TGAGGGGTGC	1440
CAGCGTGGGT	GGGCTTCTCA	GGCAGGAGGA	CATCTGGCA	GTGCTGGCTT	GGCCATTAAA	1500
TGGAAACCTG	AAGGCCAAAA	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA	1560
TTCCTGCGGC	CGC					1573

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1185 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

GAATTCGGCA	CGAGGGGGCT	TTAAGGGACA	GCTGAGCCGG	CAGGTGGCAG	ATCAGATGTG	60
GCAGGCTGGG	AAAAGACAAG	CCTCCAGGGC	CTTCAGCTTG	TACGCCAACA	TCGACATCCT	120
CAGACCCTAC	TTTGATGTGG	AGCCTGCTCA	GGTGCGAAGC	AGGCTCCTGG	AGTCCATGAT	180
CCCTATCAAG	ATGGTCAACT	TCCCCAGAA	AATTGCAGGT	GAACCTCTATG	GACCTCTCAT	240
GCTGGTCTTC	ACTCTGGTTG	CTATCCTACT	CCATGGGATG	AAGACGTCTG	ACACTATTAT	300
CCGGGAGGGC	ACCCTGATGG	GCACAGCCAT	TGGCACCTGC	TTCGGCTACT	GGCTGGGAGT	360
CTCATCCTTC	ATTTACTTCC	TTGCCTACCT	GTGCAACGCC	CAGATCACCA	TGCTGCAGAT	420
GTTGGCACTG	CTGGGCTATG	GCCTCTTTGG	GCATTGCATT	GTCCTGTTCA	TCACCTATAA	480
TATCCACCTC	CACGCCCTCT	TCTACCTCTT	CTGGCTGTTG	GTGGGTGGAC	TGTCCACACT	540
GCGCATGGTA	GCAGTGTGG	TGTCTCGGAC	CGTGGGCCCC	ACACAGCGGC	TGCTCCTCTG	600
TGGCACCCCTG	GCTGCCCTAC	ACATGCTCTT	CCTGCTCTAT	CTGCATTTTG	CCTACCACAA	660

AGTGGTAGAG GGGATCCTGG ACACACTGGA GGGCCCCAAC ATCCCGCCCA TCCAGAGGGT	720
CCCCAGAGAC ATCCCTGCCA TGCTCCCTGC TGCTCGGCTT CCCACCACCG TCCTCAACGC	780
CACAGCCAAA GCTGTTGCGG TGACCCTGCA GTCACACTGA CCCACCTGA AATTCTTGGC	840
CAGTCCTCTT TCCCGCAGCT GCAGAGAGGA GGAAGACTAT TAAAGGACAG TCCTGATGAC	900
ATGTTTCGTA GATGGGGTTT GCAGCTGCCA CTGAGCTGTA GCTGCGTAAG TACCTCCTTG	960
ATGCCTGTCTG GCACTTCTGA AAGGCACAAG GCCAAGAACT CCTGGCCAGG ACTGCAAGGC	1020
TCTGCAGCCA ATGCAGAAAA TGGGTCAGCT CCTTTGAGAA CCCCTCCCCA CCTACCCCTT	1080
CCTTCCTCTT TATCTCTCCC ACATTGTCTT GCTAAATATA GACTTGGTAA TTAAAATGTT	1140
GATTGAAGTC TGGAAAAAAA AAAAAAAAAA AATTCCTGCG GCCGC	1185

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1226 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

GAATTCGGCA CGAGGCAAGC CACCATCTTC CTTCGGCCTG CACCCCTTTA AAGGCACCCA	60
GACCCCTCTG GAAAAAGATG AACTGAAGCC CTTTGACATC CTCCAGCCTA AGGAGTACTT	120
CCAGCTCAGC CGCCACACGG TCATTAAGAT GGAAGTGAG AACGAGGCC C TGGATCTCTC	180
CATGAAGTCA GTGCCCTGGC TCAAGGCTGG TGAAGTCAGT CCCCCAATCT TCCAGGAAGA	240
TGCAGCCCTA GACCTGTCAG TGGCAGCCCA CCGGAAATCC GAGCCTCCCC CTGAGACACT	300
GTATGACAGT GGTGCATCAG TGGACAGCTC AGGTCACACA GTGATGGAGA AACTTCCCAG	360
TGGCATGGAA ATTTCTTTTG CCCCTGCCAC GTCCCATGAG GCCCCAGCCA TGATGGATAG	420
TCACATCAGC AGCAGTGATG CTGCTACCGA GATGCTCAGC CAGCCCAACC ACCCCAGCGG	480
CGAAGTCAAG GCTGAAAATA ACATTGAGAT GGTGGGCGAG TCCCAGGCGG CCAAGGTCAT	540
TGTCTCTGTC GAAGATGCTG TGCCTACCAT ATTCTGTGGC AAGATCAAAG GCCTCTCAGG	600
GGTGTCCACC AAAAATTCT CTTCAAAAG AGAAGACTCC GTGCTTCAGG GCTATGACAT	660
CAACAGCCAA GGGGAAGAGT CCATGGGAAA TGCAGAGCCC CTTAGGAAAC CCATCAAAAA	720
CCGGAGCATA AAGTTAAAGA AAGTGAATC CCAGGAAGTA CACATGCTCC CAATCAAAAA	780
ACAACGGCTG GCCACCTTTT TTCCAAGAAA GTAAATAACG GCTTTTAAA ATTTGTATGA	840
TTATAATATG GGGAAAGGTG CATTGGTTTT ATAAAAGGC ATTTAAAACA AATTATCTTT	900

GTTAATTATT TTGGGGAGTA GTTGGGAAAT GGAAAGGTGA ATTGGCTCTA GAGGCCCTGT	960
ATGCTAGTAT CATTTTCTTT TTTAATTTT GACTTTTCAC AAATGAGTAA ATAAGAGCAA	1020
CCTATTTTTC AAGCAGATTG CACATTTTTC GCAGCTTTAA TGGAATATTG GGTGAATTAG	1080
AGGGGTAAAA AAAGCTATTT TCATTGCCAC AAAGTGCTTT GATGATGTAA TACCTAATAA	1140
AGGGTAGGAT GAATATTTCA CAATAAATGT TTGTTGCAC TAAAAAAAAA AAAAAAAAAA	1200
AAAAAAAAAA AAATTCCTGC GGCCGC	1226

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1049 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

GAATTCGGCA CGAGGGCGCC ATGGTGAAGG TGACGTTCAA CTCCGCTCTG GCCCAGAAGG	60
AGGCCAAGAA GCACGAGCCC AAGAGCGGCG AGGAGGCGCT CATCATCCCC CCCGACGCCG	120
TCGCGGTGGA CTGCAAGGAC CCAGATGATG TGGTACCAGT TGGCCAAAGA AGAGCCTGGT	180
GTTGGTGCAT GTGCTTTGGA CTAGCATTTA TGCTTGCAGG TGTTATTCTA GGAGGAGCAT	240
ACTTGTACAA ATATTTTGCA CTTCAACCAG ATGACGTGTA CTACTGTGGA ATAAAGTACA	300
TCAAAGATGA TGTCACTCTA AATGAGCCCT CTGCAGATGC CCCAGCTGCT CTCTACCAGA	360
CAATTGAAGA AAATATTAAA ATCTTTGAAG AAGAAGAAGT TGAATTTATC AGTGTGCCTG	420
TCCCAGAGTT TGCAGATAGT GATCCTGCCA ACATTGTTCA TGACTTTAAC AAGAACTTA	480
CAGCCTATTT AGATCTTAAC CTGGATAAGT GCTATGTGAT CCCTCTGAAC ACTTCCATTG	540
TTATGCCACC CAGAAACCTA CTGGAGTTAC TTATTAACAT CAAGGCTGGA ACCTATTTGC	600
CTCAGTCCTA TCTGATTCAT GAGCACATGG TTATTACTGA TCGCATTGAA AACATTGATC	660
ACCTGGGTTT CTTTATTTAT CGACTGTGTC ATGACAAGGA AACTTACAAA CTGCAACGCA	720
GAGAACTAT TAAAGGTATT CAGAAACGTG AAGCCAGCAA TTGTTTCGCA ATTCGGCATT	780
TTGAAAACAA ATTTGCCGTG GAAACTTTAA TTTGTTCTTG AACAGTCAAG AAAACATTA	840
TTGAGGAAAA TTAATATCAC AGCATAACCC CACCCTTTAC ATTTTGTGTC AGTTGATTAT	900
TTTTTAAAGT CTTCTTTCAT GTAAGTAGCA AACAGGGCTT TACTATCTTT TCATCTCATT	960
AATTCAATTA AAACCATTAC CTTAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA	1020
AAAAAAAAAA AAAAAATTCC TGCGGCCCGC	1049

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1142 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

GAATTCGGCA CGAGGGGAGA ATACTTTTTG CGATGCCTAC TGGAGACTTT GATTCTGAAGC	60
CCAGTTGGGC CGACCAGGTG GAGGAGGAGG GGGAGGACGA CAAATGTGTC ACCAGCGAGC	120
TCCTCAAGGG GATCCCTCTG GCCACAGGTG ACACCAGCCC AGAGCCAGAG CTACTGCCGG	180
GAGCTCCACT GCCGCCTCCC AAGGAGGTCA TCAACGGAAA CATAAAGACA GTGACAGAGT	240
ACAAGATAGA TGAGGATGGC AAGAAGTTCA AGATTGTCCG CACCTTCAGG ATTGAGACCC	300
GGAAGGCTTC AAAGGCTGTC GCAAGGAGGA AGAACTGGAA GAAGTTCGGG AACTCAGAGT	360
TTGACCCCCC CGGACCCAAT GTGGCCACCA CCACTGTCAG TGACGATGTC TCTATGACGT	420
TCATCACCAG CAAAGAGGAC CTGAACTGCC AGGAGGAGGA GGACCCTATG AACAAATTCA	480
AGGGCCAGAA GATCGTGTCC TGCCGCATCT GCAAGGGCGA CCACTGGACC ACCCGCTGCC	540
CCTACAAGGA TACGCTGGGG CCCATGCAGA AGGAGCTGGC CGAGCAGCTG GGCCTGTCTA	600
CTGGCGAGAA GGAGAAGCTG CCGGGAGAGC TAGAGCCGGT GCAGGCCACG CAGAACAAGA	660
CAGGGAAGTA TGTGCCGCCG AGCCTGCGCG ACGGGGCCAG CCGCCGCGGG GAGTCCATGC	720
AGCCCAACCG CAGAGCCGAC GACAACGCCA CCATCCGTGT CACCAACTTG CGCAGAGGAC	780
ACGCGTGAGA CCGACCTGCA GGAGCTCTTC CGGCCTTTCG GCTCCATCTC CCGCATCTAC	840
CTGGCTAAGG ACAAGACCAC TGGCCAATCC AAGGGCTTTG CCTTCATCAG CTTCCACCGC	900
CGCGAGGATG CTGCGCGTGC CATTGCCGGG GTGTCCGGCT TTGGCTACGA CCACCTCATC	960
CTCAACGTCG AGTGGGCCAA GCCGTCCACC AACTAAGCCA GCTGCCACTG TGTA CTCCGGT	1020
CCGGGACCCCT TGGCGACAGA AGACAGCCTC CGAGAGCGCG GGCTCCAAGG GCAATAAAGC	1080
AGCTCCACTC TCAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAT TCCTGCGGCC	1140
GC	1142

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1696 base pairs

- (B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

GAATTCGGCA	CGAGGGAAAC	ATGGCGGTAG	GCTGGGACCA	TAACACAAGC	ATGACTATAT	60
GAAGGAAGAG	GAAGGTTTT	CTGAAGATGA	GGCGACTGAA	TCGGAAAAAA	ACTTTAAGTT	120
TGGTAAAAGA	GTTGGATGCC	TTTCCGAAGG	TTCCTGAGAG	CTATGTAGAG	ACTTCAGCCA	180
GTGGAGGTAC	AGTTTCTCTA	ATAGCATTTA	CAACTATGGC	TTTATTAACC	ATAATGGAAT	240
TCTCAGTATA	TCAAGATACA	TGGATGAAGT	ATGAATACGA	AGTAGACAAG	GATTTTTCTA	300
GCAAATTAAG	AATTAATATA	GATATTACTG	TTGCCATGAA	GTGTCAATAT	GTTGGAGCGG	360
ATGTATTGGA	TTTAGCAGAA	ACAATGGTTG	CATCTGCAGA	TGGTTTAGTT	TATGAACCAA	420
CAGTATTTGA	TCTTTCACCA	CAGCAGAAAG	AGTGGCAGAG	GATGCTGCAG	CTGATTGAGA	480
GTAGGCTACA	AGAAGAGCAT	TCACTTCAAG	ATGTGATATT	TAAAAGTGCT	TTTAAAAGTA	540
CATCAACAGC	TCTTCCACCA	AGAGAAGATG	ATTCATCACA	GTCTCCAAAT	GCATGCAGAA	600
TTCATGGCCA	TCTATATGTC	AATAAAGTAG	CAGGGAATTT	TCACATAACA	GTGGGCAAGG	660
CAATTCACCA	TCCTCGTGGT	CATGCACATT	TGGCAGCACT	TGTCAACCAT	GAATCTTACA	720
ATTTTTCTCA	TAGAATAGAT	CATTTGTCTT	TTGGAGAGCT	TGTTCCAGCA	ATTATTAATC	780
CTTTAGATGG	AACTGAAAAA	ATTGCTATAG	ATCACAACCA	GATGTTCCAA	TATTTTATTA	840
CAGTTGTGCC	AACAAAATA	CATACATATA	AAATATCAGC	AGACACCCAT	CAGTTTTCTG	900
TGACAGAAAG	GGAACGTATC	ATTAACCATG	CTGCAGGCAG	CCATGGAGTC	TCTGGGATAT	960
TTATGAAATA	TGATCTCAGT	TCTCTTATGG	TGACAGTTAC	TGAGGAGCAC	ATGCCATTCT	1020
GGCAGTTTTT	TGTAAGACTC	TGTGGTATTG	TTGGAGGAAT	CTTTTCAACA	ACAGGCATGT	1080
TACATGGAAT	TGGAAAATTT	ATAGTTGAAA	TAATTTGCTG	TCGTTTCAGA	CTTGGATCCT	1140
ATAAACCTGT	CAATTCTGTT	CCTTTTGAGG	ATGGCCACAC	AGACAACCAC	TTACCTCTTT	1200
TAGAAAATAA	TACACATTAA	CACCTCCCGA	TTGAAGGAGA	AAAACTTTTT	GCCTGAGACA	1260
TAAACCTTTT	TTTAAATAAT	AAAATATTGT	GCAATATATT	CAAAGAAAAG	AAAACACAAA	1320
TAAGCAGAAA	ACATACTTAT	TTTAAAAAAG	AAAAAAAAGG	ATAAAAAAAC	CCAAACTGAA	1380
ATTCTATATA	CGTTGTGTCT	GTTACAAATG	TCGTAGAAGA	AATCATGCAG	CTAAACGATG	1440
AAGAAGCCCA	ACTGGAGTGT	TGCTTTGAAG	ATGACGCCTT	CTTATATTTT	CATAGCAAAT	1500
GGGTGGTATC	AAAATCAGAC	ATTGCTTCTT	GCTGATAAAA	AGCCTGAAGG	AAATAAGTGA	1560
AACTACATCT	ATGGGAAAAA	AAAAAACATT	GAGAAGTGCA	AATGTTTCGA	TCCTTTTGTT	1620
TTTAAAAGAT	ATGATGTCAG	AATAAAATGT	GGAAAACATA	CGGAAAAAAA	AAAAAATAAA	1680
AAATTCCTGC	GGCCGC					1696

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1100 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

GAATTCGGCA	CGAGGCGGCA	CGAGGCGGCA	CGAGGGTGGC	ATATCACGGC	CATGGGGTCT	60
CAGCATTC	CTGCTGCTCG	CCCCTCCTCC	TGCAGGCGAA	AGCAAGAAGA	TGACAGGGAC	120
GGTTTGCTGG	CTGAACGAGA	GCAGGAAGAA	GCCATTGCTC	AGTTCCCATA	TGTGGAATTC	180
ACCGGGAGAG	ATAGCATCAC	CTGTCTCACG	TGCCAGGGGA	CAGGCTACAT	TCCAACAGAG	240
CAAGTAAATG	AGTTGGTGGC	TTTGATCCCA	CACAGTGATC	AGAGATTGCG	CCCTCAGCGA	300
ACTAAGCAAT	ATGTCCTCCT	GTCCATCCTG	CTTTGTCTCC	TGGCATCTGG	TTTGGTGGTT	360
TTCTTCCTGT	TTCCGCATTC	AGTCCTTG	GATGATGACG	GCATCAAAGT	GGTGAAAGTC	420
ACATTTAATA	AGCAAGACTC	CCTTGTAATT	CTCACCATCA	TGGCCACCCT	GAAAATCAGG	480
AACTCCAAC	TCTACACGGT	GGCAGTGACC	AGCCTGTCCA	GCCAGATTCA	GTACATGAAC	540
ACAGTGGTCA	GTACATATGT	GACTACTAAC	GTCTCCCTTA	TTCCACCTCG	GAGTGAGCAA	600
CTGGTGAATT	TTACCGGGAA	GGCCGAGATG	GGAGGACCGT	TTTCCTATGT	GTACTTCTTC	660
TGCACGGTAC	CTGAGATCCT	GGTGACCAAC	ATAGTGATCT	TCATGCCAAC	TCAGTGAAG	720
ATTTCATACA	TTGGCCTCAT	GACCCAGAGC	TCCTTGGAGA	CACATCACTA	TGTGGATTGT	780
GGAGGAAATT	CCACAGCTAT	TTAACAAC	CTATTGGTTC	TTCCACACAG	CGCCTGTAGA	840
AGAGAGCACA	GCATATGTTC	CCAAGGCCTG	AGTTCTGGAC	CTACCCCCAC	GTGGTGTAAG	900
CAGAGGAGGA	ATTGGTTCAC	TTAACTCCCA	GCAAACATCC	TCCTGCCACT	TAGGAGGAAA	960
CACCTCCCTA	TGGTACCATT	TATGTTTCTC	AGAACCAGCA	GAATCAGTGC	CTAGCCTGTG	1020
CCCAGCAAAT	AGTTGGCACT	CAATAAAGAT	TTGCAGAATT	TAAAAAAAAA	AAAAAAAAAA	1080
AAAAAAATTC	CTGCGGCCGC					1100

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1588 base pairs
- (B) TYPE: nucleic acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

GAATTCGGCA	CGAGGGTACC	TGCTTTTCTA	TTGCCTCTTT	GAAACAATGG	TCACGTGTTT	60
CCATGTTCCC	TACTCGGCTC	TCACCATGTT	CATCAGCACC	GAGCAGACTG	AGCGGGATTC	120
TGCCACCGCC	TATCGGATGA	CTGTGGAAGT	GCTGGGCACA	GTGCTGGGCA	CGGCGATCCA	180
GGGACAAATC	GTGGGCCAAG	CAGACACGCC	TTGTTTCCAG	GACCTCAATA	GCTCTACAGT	240
AGCTTCACAA	AGTGCCAACC	ATACACATGG	CACCACCTCA	CACAGGGAAA	CGCAAAGGC	300
ATACCTGCTG	GCAGCGGGGG	TCATTGTCTG	TATCTATATA	ATCTGTGCTG	TCATCCTGAT	360
CCTGGGCGTG	CGGGAGCAGA	GAGAACCCTA	TGAAGCCCAG	CAGTCTGAGC	CAATCGCCTA	420
CTTCGGGGGC	CTACGGCTGG	TCATGAGCCA	CGGCCCATAC	ATCAAACCTA	TTACTGGCTT	480
CCTCTTCACC	TCCTTGCTT	TCATGCTGGT	GGAGGGGAAC	TTTGCTTTGT	TTTGCACCTA	540
CACCTTGGGC	TTCCGCAATG	AATTCAGAA	TCTACTCCTG	GCCATCATGC	TCTCGGCCAC	600
TTTAACCATT	CCCATCTGGC	AGTGGTTCTT	GACCCGGTTT	GGCAAGAAGA	CAGCTGTATA	660
TGTTGGGATC	TCATCAGCAG	TGCCATTTCT	CATCTTGGTG	GCCCTCATGG	AGAGTAACCT	720
CATCATTACA	TATGCGGTAG	CTGTGGCAGC	TGGCATCAGT	GTGGCAGCTG	CCTTCTTACT	780
ACCCTGGTCC	ATGCTGCCTG	ATGTCATTGA	CGACTTCCAT	CTGAAGCAGC	CCCACTTCCA	840
TGGAACCGAG	CCCATCTTCT	TCTCCTTCTA	TGTCTTCTTC	ACCAAGTTTG	CCTCTGGAGT	900
GTCAGTGGGC	ATTTCTACCC	TCAGTCTGGA	CTTTGCAGGG	TACCAGACCC	GTGGCTGCTC	960
GCAGCCGGAA	CGTGTCAAGT	TTACACTGAA	CATGCTCGTG	ACCATGGCTC	CCATAGTTCT	1020
CATCCTGCTG	GGCCTGCTGC	TCTTCAAAAT	GTACCCCAT	GATGAGGAGA	GGCGGCGGCA	1080
GAATAAGAAG	GCCCTGCAGG	CACTGAGGGA	CGAGGCCAGC	AGCTCTGGCT	GCTCAGAAAC	1140
AGACTCCACA	GAGCTGGCTA	GCATCCTCTA	GGGCCCGCCA	CGTTGCCCCG	AGCCACCATG	1200
CAGAAGGCCA	CAGAAGGGAT	CAGGACCTGT	CTGCCGGCTT	GCTGAGCAGC	TGGACTGCAG	1260
GTGCTAGGAA	GGGAAGTGA	GAATCAAGGA	GGTGGCCCAG	GACACTTGCT	GTGCTCACTG	1320
TGGGGCCGGC	TGCTCTGTGG	CCTCCTGCCT	CCCCTCTGCC	TGCCTGTGGG	GCCAAGCCCT	1380
GGGGCTGCCA	CTGTGAATAT	GCCAAGGACT	GATCGGGCCT	AGCCCGGAAC	ACTAATGTAG	1440
AAACCTTTTT	TTTACAGAGC	CTAATTAATA	ACTTAATGAC	TGTGTACATA	GCAATGTGTG	1500
TGTATGTATA	TGTCTGTGAG	CTATTAATGT	TATTAATTTT	CATAAAAGCT	GGAAAGCAAA	1560
AAAAAAAAAA	AAAAATTCCT	GCGGCCGC				1588

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1535 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

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GAATTCGGCA CGAGGCGGAA GTCCCGTCTC ACGGTTGCCC TGGCAGCGCG CGAGGCTGGT      60
GAGTCGGCAG CCCTGTGGCA GCCGGCGGGC TGGTTTCCAT GGTTCACGA TTAGGAACCA      120
CCAGCTGCTG CATCCCATGG CCAGGGGTGG CGTCCAGGTG GCAGAGCAGC TAGGAACGCA      180
AGGCCTGAAC CTGGGGCCAG ACACCCTGCT CTCCCGGCCA TGGTCAACGA CCCTCCAGTA      240
CCTGCCTTAC TGTGGGCCCA GGAGGTGGGC CAAGTCTTGG CAGGCCGTGC CCGCAGGCTG      300
CTGCTGCAGT TTGGGGTGCT CTTCTGCACC ATCCTCCTTT TGCTCTGGGT GTCTGTCTTC      360
CTCTATGGCT CCTTCTACTA TTCCTATATG CCGACAGTCA GCCACCTCAG CCCTGTGCAT      420
TTCTACTACA GGACCGACTG TGATTCCCTC ACCACCTCAC TCTGCTCCTT CCCTGTTGCC      480
AATGTCTCGC TGAATAAGGG TGGACGTGAT CGGGTGCTGA TGTATGGACA GCCGTATCGT      540
GTTACCTTAG AGCTTGAGCT GCCAGAGTCC CCTGTGAATC AAGATTTGGG CATGTTCTTG      600
GTCACCATTT CCTGCTACAC CAGAGGTGGC CGAATCATCT CCACTTCTTC GCGTTCGGTG      660
ATGCTGCATT ACCGCTCAGA CCTGCTCCAG ATGCTGGACA CACTGGTCTT CTCTAGCCTC      720
CTGCTATTTG GCTTTGCAGA GCAGAAGCAG CTGCTGGAGG TGGAACCTA CGCAGACTAT      780
AGAGAGAACT CGTACGTGCC GACCACTGGA GCGATCATTG AGATCCACAG CAAGCGCATC      840
CAGCTGTATG GAGCCTACCT CCGCATCCAC GCGCACTTCA CTGGGCTCAG ATACCTGCTA      900
TACAACTTCC CGATGACCTG CGCCTTCATA GGTGTTGCCA GCAACTTCAC CTTCTCAGC      960
GTCATCGTGC TCTTCAGCTA CATGCAGTGG GTGTGGGGGG GCATCTGGCC CCGACACCGC     1020
TTCTCTTTGC AGGTTAACAT CCGAAAAAGA GACAATTCCC GGAAGGAAGT CCAACGAAGG     1080
ATCTCTGCTC ATCAGCCAGG GCCTGAAGGC CAGGAGGAGT CAACTCCGCA ATCAGATGTT     1140
ACAGAGGATG GTGAGAGCCC TGAAGATCCC TCAGGGACAG AGGTCAGCTG TCCGAGGAGG     1200
AGAAACCAGA TCAGCAGCCC CTGAGCGGAG AAGAGGAGCT AGAGCCTGAG GCCAGTGATG     1260
GTTCAGGCTC CTGGGAAGAT GCAGCTTTGC TGACGGAGGC CAACCTGCCT GCTCCTGCTC     1320
CTGCTTCTGC TTCTGCCCCCT GTCCTAGAGA CTCTGGGCAG CTCTGAACCT GCTGGGGGTG     1380
CTCTCCGACA GCGCCCCACC TGCTCTAGTT CCTGAAGAAA AGGGGCAGAC TCCTCACATT     1440
CCAGCACTTT CCCACCTGAC TCCTCTCCCC TCGTTTTTCC TTCAATAAAC TATTTTGTGT     1500
CAAAAAAAAA AAAAAAAAAA AATTCCTGCG GCCGC                                     1535

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(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1322 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

GAATTCGGCA	CGAGGGCGGG	CGCTACGGGC	TTGACTCCCC	CAAGGCCGAG	GTCCGCGGCC	60
AGGTGCTGGC	GCCGCTGCCC	CTCCACGGAG	TTGCTGATCA	TCTGGGCTGT	GATCCACAAA	120
CCCGGTTCTT	TGTCCCTCCT	AATATCAAAC	AGTGGATTGC	CTTGCTGCAG	AGGGGAAACT	180
GCACGTTTAA	AGAGAAAATA	TCACGGGCCG	CTTCCACAA	TGCAGTTGCT	GTAGTCATCT	240
ACAATAATAA	ATCCAAAGAG	GAGCCAGTTA	CCATGACTCA	TCCAGGCACT	GGAGATATTA	300
TTGCTGTCA	GATAACAGAA	TTGAGGGGTA	AGGATATTTT	GAGTTATCTG	GAGAAAAACA	360
TCTCTGTACA	AATGACAATA	GCTGTTGGAA	CTCGAATGCC	ACCGAAGAAC	TTCAGCCGTG	420
GCTCTCTAGT	CTTCGTGTCA	ATATCCTTTA	TTGTTTTGAT	GATTATTTCT	TCAGCATGGC	480
TCATATTCTA	CTTCATTCAA	AAGATCAGGT	ACACAAATGC	ACGCGACAGG	AACCAGCGTC	540
GTCTCGGAGA	TGCAGCCAAG	AAAGCCATCA	GTAAATTGAC	AACCAGGACA	GTAAAGAAGG	600
GTGACAAGGA	AACTGACCCA	GACTTTGATC	ATTGTGCAGT	CTGCATAGAG	AGCTATAAGC	660
AGAATGATGT	CGTCCGAATT	CTCCCCTGCA	AGCATGTTTT	CCACAAATCC	TGCGTGGATC	720
CCTGGCCTAG	TGAACATTGT	ACCTGTCCTA	TGTGCAAAC	TAATATATTG	AAGGCCCTGG	780
GAATTGTGCC	GAATTTGCCA	TGTACTGATA	ACGTAGCATT	CGATATGGAA	AGGCTCACCA	840
GAACCCAAGC	TGTTAACCGA	AGATCAGCCC	TCGGCGACCT	CGCCGGCGAC	AACTCCCTTG	900
GCCTTGAGCC	ACTTCGAACT	TCGGGGATCT	CACCTCTTCC	TCAGGATGGG	GAGCTCACTC	960
CGAGAACAGG	AGAAATCAAC	ATTGCAGTAA	CAAAAGAATG	GTTTATTATT	GCCAGTTTTG	1020
GCCTCCTCAG	TGCCCTCACA	CTCTGCTACA	TGATCATCAG	AGCCACAGCT	AGCTTGAATG	1080
CTAATGAGGT	AGAATGGTTT	TGAAGAAGAA	AAAACCTGCT	TTCTGACTGA	TTTTGCCTTG	1140
AAGGAAAAAA	GAACCTATTT	TTGTGCATCA	TTTACCAATC	ATGCCACACA	AGCATTATTT	1200
TTTAGTACAT	TTTATTTTTT	CATAAAATTG	CTAATGCCAA	AGCTTTGTAT	TAAAGAAAT	1260
AAATAATAAA	ATAAAAAAAA	AAAAAAAAAA	AAAAAAAAAA	AAAAAAAAT	TCCTGCGGCC	1320
GC						1322

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1711 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

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GAATTCGGCA CGAGGCCCTC CCGCGCTCCC GGGGCGCGCG GGCCGCGCCC CCGACGCCCT      60
ACATATACTC AGGTGCGCCC CACCTGTCCG CCCGCACCTG CTGGCTCACC TCCGAGCCAC      120
CTCTGCTGCG CACCGCAGCC TCGGACCTAC AGCCCAGGAT ACTTTGGGAC TTGCCGGCGC      180
TCAGAAACGC GCCCAGACGG CCCCTCCACC TTTTGTTTGC CTAGGGTCGC CGAGAGCGCC      240
CGGAGGGAAC CGCCTGGCCT TCGGGGACCA CCAATTTTGT CTGGAACCAC CCTCCCGGCG      300
TATCCTACTC CCTGTGCCGC GAGGCCATCG CTTCACTGGA GGGGTCGATT TGTGTGTAGT      360
TTGGTGACAA GATTTGCATT CACCTGGCCC AAACCCTTTT TGTCTCTTTG GGTGACCGGA      420
AAACTCCACC TCAAGTTTTC TTTTGTGGGG CTGCCCCCCA AGTGTCGTTT GTTTTACTGT      480
AGGGTCTCCC GCCCGGCGCC CCCAGTGTTT TCTGAGGGCG GAAATGGCCA ATTCGGGCCT      540
GCAGTTGCTG GGCTTCTCCA TGGCCCTGCT GGGCTGGGTG GGTCTGGTGG CCTGCACCGC      600
CATCCCGCAG TGGCAGATGA GCTCCTATGC GGGTGACAAC ATCATCACGG CCCAGGCCAT      660
GTACAAGGGG CTGTGGATGG ACTGCGTCAC GCAGAGCAGC GGGATGATGA GCTGCAAAAT      720
GTACGACTCG GTGCTCGCCC TGTCCGCGGC CTTGCAGGCC ACTCGAGCCC TAATGGTGGT      780
CTCCCTGGTG CTGGGCTTCC TGGCCATGTT TGTGGCCACG ATGGGCATGA AGTGCACGCG      840
CTGTGGGGGA GACGACAAAG TGAAGAAGGC CCGTATAGCC ATGGGTGGAG GCATAATTTT      900
CATCGTGGCA GGTCTTGCCG CCTTGGTAGC TTGCTCCTGG TATGGCCATC AGATTGTCAC      960
AGACTTTTAT AACCCTTTGA TCCCTACCAA CATTAAGTAT GAGTTTGGCC CTGCCATCTT     1020
TATTGGCTGG GCAGGGTCTG CCCTAGTCAT CCTGGGAGGT GCACTGCTCT CCTGTTCCCTG     1080
TCCTGGGAAT GAGAGCAAGG CTGGGTACCG TGCACCCCGC TCTTACCCTA AGTCCAACTC     1140
TTCCAAGGAG TATGTGTGAC CTGGGATCTC CTTGCCCCAG CCTGACAGGC TATGGGAGTG     1200
TCTAGATGCC TGAAAGGGCC TGGGGCTGAG CTCAGCCTGT GGGCAGGGTG CCGGACAAAG     1260
GCCTCCTGGT CACTCTGTCC CTGCACTCCA TGTATAGTCC TCTTGGGTTG GGGGTGGGGG     1320
GGTGCCGTTG GTGGGAGAGA CAAAAGAGG GAGAGTGTGC TTTTGTACA GTAATAAAAA     1380
ATAAGTATTG GGAAGCAGGC TTTTTCCTC TCAGGGCCTC TGCTTTCCTC CCGTCCAGAT     1440
CCTTGCAAGG AGCTTGGAAC CTTAGTGCAC CTACTTCAGT TCAGAACTAG TAGCACCCCA     1500
CTGACTCCAC TGACAATTGA CTAAAAGATG CAGGTGCTCG TATCTCGACA TTCATTCCCA     1560
CCCCCTCTT ATTTAAATAG CTACCAAAGT ACTTCTTTTT TAATAAAAAA ATAAAGATTT     1620
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TTATTAGGTA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA AAAAAAAAAA 1680
AAAAAAAAAA AAAAAAATT CCTGCGGCCG C 1711

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1553 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

GAATTCGGCA	CGAGGGCAGG	TCCAGAGTAA	AGTCACTGAA	GAGTGAAGC	GAGGAAGGAA	60
CAGGATGATT	AGACCTCAGC	TGCGGACCGC	GGGGCTGGGA	CGATGCCTCC	TGCCGGGGCT	120
GCTGCTGCTC	CTGGTGCCCG	TCCTCTGGGC	CGGGGCTGAA	AAGCTACATA	CCCAGCCCTC	180
CTGCCCCGCG	GTCTGCCAGC	CCACGCGCTG	CCCCGCGCTG	CCCACCTGCG	CGCTGGGGAC	240
CACGCCGGTG	TTGACCTGT	GCCGCTGTTG	CCGCGTCTGC	CCCGCGGCCG	AGCGTGAAGT	300
CTGCGGCGGG	GCGCAGGGCC	AACCGTGCGC	CCCGGGGCTG	CAGTGCCTCC	AGCCGCTGCG	360
CCCCGGGTTC	CCCAGCACCT	GCGGTTGCCC	GACGCTGGGA	GGGGCCGTGT	GCGGCAGCGA	420
CAGGCGCACC	TACCCAGCA	TGTGCGCGCT	CCGGGCCGAA	AACCGCGCCG	CGCGCCGCCT	480
GGGCAAGGTC	CCGGCCGTGC	CTGTGCAGTG	GGGGAAGTGC	GGGGATACAG	GGACCAGAAG	540
CGCAGGCCCC	CTCAGGAGGA	ATTACAACCT	CATCGCCGCG	GTGGTGGAGA	AGGTGGCGCC	600
ATCGGTGGTT	CACGTGCAGC	TGTGGGGCAG	GTTACTTCAC	GGCAGCAGGC	TTGTTCTCTGT	660
GTACAGTGGC	TCTGGGTTCA	TAGTGTCTGA	GGACGGGCTC	ATTATTACCA	ATGCCCATGT	720
TGTCAGGAAC	CAGCAGTGGA	TTGAGGTGGT	GCTCCAGAAT	GGGGCCCGTT	ATGAAGCTGT	780
TGTCAAGGAT	ATTGACCTTA	AATTGGATCT	TGCGGTGATT	AAGATTGAAT	CAAATGCTGA	840
ACTTCCTGTA	CTGATGCTGG	GAAGATCATC	TGACCTTCGG	GCTGGAGAGT	TTGTGGTGGC	900
TTTGGGCAGC	CCATTTTCTC	TGCAGAACAC	AGCTACTGCA	GGAATTGTCA	GCACCAAACA	960
GCGAGGGGGC	AAAGAACTGG	GGATGAAGGA	TTCAGATATG	GACTACGTCC	AGATTGATGC	1020
CACAATTAAC	TATGGGAATT	CTGGTGGTCC	TCTGGTGAAC	TTGGATGGTG	ATGTGATTGG	1080
CGTCAATTCA	TTGAGGGTGA	CTGATGGAAT	CTCCTTTGCA	ATTCCTTCAG	ATCGAGTTAG	1140
GCAGTTCTTG	GCAGAATACC	ATGAGCACCA	GATGAAAGGA	AAGGCGTTTT	CAAATAAGAA	1200
ATATCTGGGT	CTGCAATGTC	TGTCCCTCAC	TGTGCCCCCT	AGTGAAGAAT	TGAAAATGCA	1260
TTATCCAGAT	TTCCCTGATG	TGAGTTCTGG	GGTTTATGTA	TGTAAAGTGG	TTGAAGGAAC	1320

AGCTGCTCAA AGCTCTGGAT TGAGAGATCA CGATGTAATT GTCAACATAA ATGGGAAACC 1380
TATTACTACT ACAACTGATG TTGTTAAAGC TCTTGACAGT GATTCCCTTT CCATGGCTGT 1440
TCTTCGGGGA AAAGATAATT TGCTCCTGAC AGTCATACCT GAAACAATCA ATTAAATATC 1500
TTGTTTAAA GTGGGATTAT CTAAAAAAA AAAAAAAA TTCCTGCGGC CGC 1553

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1596 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

GAATTCGGCA CGAGGGGAGC CGCTCCCGGA GCCCGGCCGT AGAGGCTGCA ATCGCAGCCG 60
GGAGCCCGCA GCCCGCGCCC CGAGCCCGCC GCCGCCCTTC GAGGGCGCCC CAGGCCGCGC 120
CATGGTGAAG GTGACGTTCA ACTCCGCTCT GGCCAGAAAG GAGGCCAAGA AGGACGAGCC 180
CGAGAGCGGC GAGGAGGCGC TCATCATCCC CCCCAGCGCC GTCGCGGTGG ACTGCAAGGA 240
CCCAGATGAT GTGGTACCAG TTGGCCAAAG AAGAGCCTGG TGTGGTGCA TGTGCTTTGG 300
ACTAGCATTT ATGCTTGCAAG GTGTTATTCT AGGAGGAGCA TACTTGTAACA AATATTTTGC 360
ACTTCAACCA GATGACGTGT ACTACTGTGG AATAAAGTAC ATCAAAGATG ATGTCATCTT 420
AAATGAGCCC TCTGCAGATG CCCAGCTGC TCTCTACCAG ACAATTGAAG AAAATATTAA 480
AATCTTTGAA GAAGAAGAAG TTGAATTTAT CAGTGTGCCT GTCCCAGAGT TTGCAGATAG 540
TGATCCTGCC AACATTGTTT ATGACTTTAA CAAGAACTT ACAGCCTATT TAGATCTTAA 600
CCTGGATAAG TGCTATGTGA TCCCTCTGAA CACTTCCATT GTTATGCCAC CCAGAAACCT 660
ACTGGAGTTA CTTATTAAACA TCAAGGCTGG AACCTATTTG CCTCAGTCCT ATCTGATTCA 720
TGAGCACATG GTTATTACTG ATCGCATTGA AAACATTGAT CACCTGGGTT TCTTTATTTA 780
TCGACTGTGT CATGACAAGG AAAGTTACAA ACTGCAACGC AGAGAACTA TTAAAGGTAT 840
TCAGAAACGT GAAGCCAGCA ATTGTTTCGC AATTCGGCAT TTTGAAAACA AATTGCCGT 900
GGAAACTTTA ATTTGTTCTT GAACAGTCAA GAAAAACATT ATTGAGGAAA ATTAATATCA 960
CAGCATAACC CCACCCTTTA CATTTTGTGC AGTGATATTT TTTAAAGTCT CTTTCATGTA 1020
AGTAGCAAAC AGGGCTTTAC TATCTTTTCA TCTCATTAAT TCAATTAAAA CCATTACCTT 1080
AAAATTTTTT TCTTTCGAAG TGTGGTGTCT TTTATATTTG AATTAGTAAC TGTATGAAGT 1140


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CATAGATAAT AGTACATGTC ACCTTAGGTA GTAGGAAGAA TTACAATTTT TTTAAATCAT 1200
TTATCTGGAT TTTTATGTTT TATTAGCATT TTCAAGAAGA CGGATTATCT AGAGAATAAT 1260
CATATATATG CATACGTAAA AATGGACCAC AGTGACTTAT TTGTAGTTGT TAGTTGCCCT 1320
GCTACCTAGT TTGTTAGTGC ATTTGAGCAC ACATTTTAAAT TTTCTCTCTAA TTAAAATGTG 1380
CAGTATTTTC AGTGTCAAAT ATATTTAACT ATTTAGAGAA TGATTTCCAC CTTTATGTTT 1440
TAATATCCTA GGCATCTGCT GTAATAATAT TTTAGAAAAT GTTTGGAATT TAAGAAATAA 1500
CTTGTGTTAC TAATTTGTAT AACCCATATC TGTGCAATGG AATATAAATA TCACAAAGTT 1560
GTTTAAAAAA AAAAAAAAAA AAATTCCTGC GGCCGC 1596

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(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 400 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

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Met Ala Trp Arg Arg Arg Glu Ala Gly Val Gly Ala Arg Gly Val Leu
 1             5             10             15
Ala Leu Ala Leu Leu Ala Leu Ala Leu Cys Val Pro Gly Ala Arg Gly
 20             25             30
Arg Ala Leu Glu Trp Phe Ser Ala Val Val Asn Ile Glu Tyr Val Asp
 35             40             45
Pro Gln Thr Asn Leu Thr Val Trp Ser Val Ser Glu Ser Gly Arg Phe
 50             55             60
Gly Asp Ser Ser Pro Lys Glu Gly Ala His Gly Leu Val Gly Val Pro
 65             70             75             80
Trp Ala Pro Gly Gly Asp Leu Glu Gly Cys Ala Pro Asp Thr Arg Phe
 85             90             95
Phe Val Pro Glu Pro Gly Gly Arg Gly Ala Ala Pro Trp Val Ala Leu
100             105             110
Val Ala Arg Gly Gly Cys Thr Phe Lys Asp Lys Val Leu Val Ala Ala

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115	120	125
Arg Arg Asn Ala Ser Ala Val Val Leu Tyr Asn Glu Glu Arg Tyr Gly		
130	135	140
Asn Ile Thr Leu Pro Met Ser His Ala Gly Thr Gly Asn Ile Val Val		
145	150	155
Ile Met Ile Ser Tyr Pro Lys Gly Arg Glu Ile Leu Glu Leu Val Gln		
165	170	175
Lys Gly Ile Pro Val Thr Met Thr Ile Gly Val Gly Thr Arg His Val		
180	185	190
Gln Glu Phe Ile Ser Gly Gln Ser Val Val Phe Val Ala Ile Ala Phe		
195	200	205
Ile Thr Met Met Ile Ile Ser Leu Ala Trp Leu Ile Phe Tyr Tyr Ile		
210	215	220
Gln Arg Phe Leu Tyr Thr Gly Ser Gln Ile Gly Ser Gln Ser His Arg		
225	230	235
Lys Glu Thr Lys Lys Val Ile Gly Gln Leu Leu Leu His Thr Val Lys		
245	250	255
His Gly Glu Lys Gly Ile Asp Val Asp Ala Glu Asn Cys Ala Val Cys		
260	265	270
Ile Glu Asn Phe Lys Val Lys Asp Ile Ile Arg Ile Leu Pro Cys Lys		
275	280	285
His Ile Phe His Arg Ile Cys Ile Asp Pro Trp Leu Leu Asp His Arg		
290	295	300
Thr Cys Pro Met Cys Lys Leu Asp Val Ile Lys Ala Leu Gly Tyr Trp		
305	310	315
Gly Glu Pro Gly Asp Val Gln Glu Met Pro Ala Pro Glu Ser Pro Pro		
325	330	335
Gly Arg Asp Pro Ala Ala Asn Leu Ser Leu Ala Leu Pro Asp Asp Asp		
340	345	350
Gly Ser Asp Asp Ser Ser Pro Pro Ser Ala Ser Pro Ala Glu Ser Glu		
355	360	365
Pro Gln Cys Asp Pro Ser Phe Lys Gly Asp Ala Gly Glu Asn Thr Ala		
370	375	380
Leu Leu Glu Ala Gly Arg Ser Asp Ser Arg His Gly Gly Pro Ile Ser		
385	390	395
		400

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 291 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

```

Met Asp Lys Gly Ser Ala Gly His Pro Gly Gly Val Leu Val Trp Gly
 1             5             10             15
Arg Ser Pro Ala Pro Thr Ala Leu Trp Gly Ala Ser Pro Trp Leu Ser
      20             25             30
Pro Leu Thr Ser Ala Leu Arg Gln Pro Leu His Arg Ala Pro Leu Leu
      35             40             45
Pro Gly Gln Leu Cys Trp Ser Pro Arg Pro Leu Glu Lys Asn Lys Ala
      50             55             60
Met Gly Arg Pro Leu Leu Leu Pro Leu Leu Leu Leu Leu Gln Pro Pro
65             70             75             80
Ala Phe Leu Gln Pro Gly Gly Ser Thr Gly Ser Gly Pro Ser Tyr Leu
      85             90             95
Tyr Gly Val Thr Gln Pro Lys His Leu Ser Ala Ser Met Gly Gly Ser
      100            105            110
Val Glu Ile Pro Phe Ser Phe Tyr Tyr Pro Trp Glu Leu Ala Ile Val
      115            120            125
Pro Asn Val Arg Ile Ser Trp Arg Arg Gly His Phe His Gly Gln Ser
      130            135            140
Phe Tyr Ser Thr Arg Pro Pro Ser Ile His Lys Asp Tyr Val Asn Arg
145            150            155            160
Leu Phe Leu Asn Trp Thr Glu Gly Gln Glu Ser Gly Phe Leu Arg Ile
      165            170            175
Ser Asn Leu Arg Lys Glu Asp Gln Ser Val Tyr Phe Cys Arg Val Glu
      180            185            190

```

Leu Asp Thr Arg Arg Ser Gly Arg Gln Gln Leu Gln Ser Ile Lys Gly
 195 200 205
 Thr Lys Leu Thr Ile Thr Gln Ala Val Thr Thr Thr Thr Thr Trp Arg
 210 215 220
 Pro Ser Ser Thr Thr Thr Ile Ala Gly Leu Arg Val Thr Glu Ser Lys
 225 230 235 240
 Gly His Ser Glu Ser Trp His Leu Ser Leu Asp Thr Ala Ile Arg Val
 245 250 255
 Ala Leu Ala Val Ala Val Leu Lys Thr Val Ile Leu Gly Leu Leu Cys
 260 265 270
 Leu Leu Leu Leu Trp Trp Arg Arg Arg Lys Gly Ser Arg Ala Pro Ser
 275 280 285
 Ser Asp Phe
 290

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 293 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Met Thr Val Ser Gln Arg Phe Gln Leu Ser Asn Ser Gly Pro Asn Ser
 1 5 10 15
 Thr Ile Lys Met Lys Ile Ala Leu Arg Val Leu His Leu Glu Lys Arg
 20 25 30
 Glu Arg Pro Pro Asp His Gln His Ser Ala Gln Val Lys Arg Pro Ser
 35 40 45
 Val Ser Lys Glu Gly Arg Lys Thr Ser Ile Lys Ser His Met Ser Gly
 50 55 60
 Ser Pro Gly Pro Gly Gly Ser Asn Thr Ala Pro Ser Thr Pro Val Ile

```

65              70              75              80
Gly Gly Ser Asp Lys Pro Gly Met Glu Glu Lys Ala Gln Pro Pro Glu
      85              90              95
Ala Gly Pro Gln Gly Leu His Asp Leu Gly Arg Ser Ser Ser Ser Leu
      100             105             110
Leu Ala Ser Pro Gly His Ile Ser Val Lys Glu Pro Thr Pro Ser Ile
      115             120             125
Ala Ser Asp Ile Ser Leu Pro Ile Ala Thr Gln Glu Leu Arg Gln Arg
      130             135             140
Leu Arg Gln Leu Glu Asn Gly Thr Thr Leu Gly Gln Ser Pro Leu Gly
      145             150             155             160
Gln Ile Gln Leu Thr Ile Arg His Ser Ser Gln Arg Asn Lys Leu Ile
      165             170             175
Val Val Val His Ala Cys Arg Asn Leu Ile Ala Phe Ser Glu Asp Gly
      180             185             190
Ser Asp Pro Tyr Val Arg Met Tyr Leu Leu Pro Asp Lys Arg Arg Ser
      195             200             205
Gly Arg Arg Lys Thr His Val Ser Lys Lys Thr Leu Asn Pro Val Phe
      210             215             220
Asp Gln Ser Phe Asp Phe Ser Val Ser Leu Pro Glu Val Gln Arg Arg
      225             230             235             240
Thr Leu Asp Val Ala Val Lys Asn Ser Gly Gly Phe Leu Ser Lys Asp
      245             250             255
Lys Gly Leu Leu Gly Lys Val Leu Val Ala Leu Ala Ser Glu Glu Leu
      260             265             270
Ala Lys Gly Trp Thr Gln Trp Tyr Asp Leu Thr Glu Asp Gly Thr Arg
      275             280             285
Pro Gln Ala Met Thr
      290

```

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 206 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

Met	Glu	Arg	Arg	His	Pro	Val	Cys	Ser	Gly	Thr	Cys	Gln	Pro	Thr	Gln
1				5					10					15	
Phe	Arg	Cys	Ser	Asn	Gly	Cys	Cys	Ile	Asp	Ser	Phe	Leu	Glu	Cys	Asp
				20				25					30		
Asp	Thr	Pro	Asn	Cys	Pro	Asp	Ala	Ser	Asp	Glu	Ala	Ala	Cys	Glu	Lys
				35				40					45		
Tyr	Thr	Ser	Gly	Phe	Asp	Glu	Leu	Gln	Arg	Ile	His	Phe	Pro	Ser	Asp
				50				55				60			
Lys	Gly	His	Cys	Val	Asp	Leu	Pro	Asp	Thr	Gly	Leu	Cys	Lys	Glu	Ser
65				70				75					80		
Ile	Pro	Arg	Trp	Tyr	Tyr	Asn	Pro	Phe	Ser	Glu	His	Cys	Ala	Arg	Phe
				85				90					95		
Thr	Tyr	Gly	Gly	Cys	Tyr	Gly	Asn	Lys	Asn	Asn	Phe	Glu	Glu	Glu	Gln
				100				105					110		
Gln	Cys	Leu	Glu	Ser	Cys	Arg	Gly	Ile	Ser	Lys	Lys	Asp	Val	Phe	Gly
				115				120				125			
Leu	Arg	Arg	Glu	Ile	Pro	Ile	Pro	Ser	Thr	Gly	Ser	Val	Glu	Met	Ala
				130				135				140			
Val	Ala	Val	Phe	Leu	Val	Ile	Cys	Ile	Val	Val	Val	Val	Ala	Ile	Leu
145				150				155					160		
Gly	Tyr	Cys	Phe	Phe	Lys	Asn	Gln	Arg	Lys	Asp	Phe	His	Gly	His	His
				165				170					175		
His	His	Pro	Pro	Pro	Thr	Pro	Ala	Ser	Ser	Thr	Val	Ser	Thr	Thr	Glu
				180				185					190		
Asp	Thr	Glu	His	Leu	Val	Tyr	Asn	His	Thr	Thr	Arg	Pro	Leu		
				195				200					205		

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 220 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

```

Met Ala Gly Leu Ser Arg Gly Ser Ala Arg Ala Leu Leu Ala Ala Leu
 1           5           10           15
Leu Ala Ser Thr Leu Leu Ala Leu Leu Val Ser Pro Ala Arg Gly Arg
      20           25           30
Gly Gly Arg Asp His Gly Asp Trp Asp Glu Ala Ser Arg Leu Pro Pro
      35           40           45
Leu Pro Pro Arg Glu Asp Ala Ala Arg Val Ala Arg Phe Val Thr His
      50           55           60
Val Ser Asp Trp Gly Ala Leu Ala Thr Ile Ser Thr Leu Glu Ala Val
      65           70           75           80
Arg Gly Arg Pro Phe Ala Asp Val Leu Ser Leu Ser Asp Gly Pro Pro
      85           90           95
Gly Ala Gly Ser Gly Val Pro Tyr Phe Tyr Leu Ser Pro Leu Gln Leu
      100          105          110
Ser Val Ser Asn Leu Gln Glu Asn Pro Tyr Ala Thr Leu Thr Met Thr
      115          120          125
Leu Ala Gln Thr Asn Phe Cys Lys Lys His Gly Phe Asp Pro Gln Ser
      130          135          140
Pro Leu Cys Val His Ile Met Leu Ser Gly Thr Val Thr Lys Val Asn
      145          150          155          160
Glu Thr Glu Met Asp Ile Ala Lys His Ser Leu Phe Ile Arg His Pro
      165          170          175
Glu Met Lys Thr Trp Pro Ser Ser His Asn Trp Phe Phe Ala Lys Leu
      180          185          190
Asn Ile Thr Asn Ile Trp Val Leu Asp Tyr Phe Gly Gly Pro Lys Ile
      195          200          205
Val Thr Pro Glu Glu Tyr Tyr Asn Val Thr Val Gln
  
```

210

215

220

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 197 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

Met Asp His His Cys Pro Trp Leu Asn Asn Cys Val Gly His Tyr Asn
1 5 10 15
His Arg Tyr Phe Phe Ser Phe Cys Phe Phe Met Thr Leu Gly Cys Val
20 25 30
Tyr Cys Ser Tyr Gly Ser Trp Asp Leu Phe Arg Glu Ala Tyr Ala Ala
35 40 45
Ile Glu Lys Met Lys Gln Leu Asp Lys Asn Lys Leu Gln Ala Val Ala
50 55 60
Asn Gln Thr Tyr His Gln Thr Pro Pro Pro Thr Phe Ser Phe Arg Glu
65 70 75 80
Arg Met Thr His Lys Ser Leu Val Tyr Leu Trp Phe Leu Cys Ser Ser
85 90 95
Val Ala Leu Ala Leu Gly Ala Leu Thr Val Trp His Ala Val Leu Ile
100 105 110
Ser Arg Gly Glu Thr Ser Ile Glu Arg His Ile Asn Lys Lys Glu Arg
115 120 125
Arg Arg Leu Gln Ala Lys Gly Arg Val Phe Arg Asn Pro Tyr Asn Tyr
130 135 140
Gly Cys Leu Asp Asn Trp Lys Val Phe Leu Gly Val Asp Thr Gly Arg
145 150 155 160
His Trp Leu Thr Arg Val Leu Leu Pro Ser Thr His Leu Pro His Gly
165 170 175

Asn Gly Met Ser Trp Glu Pro Pro Pro Trp Val Thr Ala His Ser Ala
 180 185 190
 Ser Val Met Ala Val
 195

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 451 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Met Ala Pro Leu Gly Met Leu Leu Gly Leu Leu Met Ala Ala Cys Phe
 1 5 10 15
 Thr Phe Cys Leu Ser His Gln Asn Leu Lys Glu Phe Ala Leu Thr Asn
 20 25 30
 Pro Glu Lys Ser Ser Thr Lys Glu Thr Glu Arg Lys Glu Thr Lys Ala
 35 40 45
 Glu Glu Glu Leu Asp Ala Glu Val Leu Glu Val Phe His Pro Thr His
 50 55 60
 Glu Trp Gln Ala Leu Gln Pro Gly Gln Ala Val Pro Ala Gly Ser His
 65 70 75 80
 Val Arg Leu Asn Leu Gln Thr Gly Glu Arg Glu Ala Lys Leu Gln Tyr
 85 90 95
 Glu Asp Lys Phe Arg Asn Asn Leu Lys Gly Lys Arg Leu Asp Ile Asn
 100 105 110
 Thr Asn Thr Tyr Thr Ser Gln Asp Leu Lys Ser Ala Leu Ala Lys Phe
 115 120 125
 Lys Glu Gly Ala Glu Met Glu Ser Ser Lys Glu Asp Lys Ala Arg Gln
 130 135 140
 Ala Glu Val Lys Arg Leu Phe Arg Pro Ile Glu Glu Leu Lys Lys Asp

145	150	155	160
Phe Asp Glu Leu Asn Val Val Ile Glu Thr Asp Met Gln Ile Met Val			
165	170	175	
Arg Leu Ile Asn Lys Phe Asn Ser Ser Ser Ser Ser Leu Glu Glu Lys			
180	185	190	
Ile Ala Ala Leu Phe Asp Leu Glu Tyr Tyr Val His Gln Met Asp Asn			
195	200	205	
Ala Gln Asp Leu Leu Ser Phe Gly Gly Leu Gln Val Val Ile Asn Gly			
210	215	220	
Leu Asn Ser Thr Glu Pro Leu Val Lys Glu Tyr Ala Ala Phe Val Leu			
225	230	235	240
Gly Ala Ala Phe Ser Ser Asn Pro Lys Val Gln Val Glu Ala Ile Glu			
245	250	255	
Gly Gly Ala Leu Gln Lys Leu Leu Val Ile Leu Ala Thr Glu Gln Pro			
260	265	270	
Leu Thr Ala Lys Lys Lys Val Leu Phe Ala Leu Cys Ser Leu Leu Arg			
275	280	285	
His Phe Pro Tyr Ala Gln Arg Gln Phe Leu Lys Leu Gly Gly Leu Gln			
290	295	300	
Val Leu Arg Thr Leu Val Gln Glu Lys Gly Thr Glu Val Leu Ala Val			
305	310	315	320
Arg Val Val Thr Leu Leu Tyr Asp Leu Val Thr Glu Lys Met Phe Ala			
325	330	335	
Glu Glu Glu Ala Glu Leu Thr Gln Glu Met Ser Pro Glu Lys Leu Gln			
340	345	350	
Gln Tyr Arg Gln Val His Leu Leu Pro Gly Leu Trp Glu Gln Gly Trp			
355	360	365	
Cys Glu Ile Thr Ala His Leu Leu Ala Leu Pro Glu His Asp Ala Arg			
370	375	380	
Glu Lys Val Leu Gln Thr Leu Gly Val Leu Leu Thr Thr Cys Arg Asp			
385	390	395	400
Arg Tyr Arg Gln Asp Pro Gln Leu Gly Arg Thr Leu Ala Ser Leu Gln			
405	410	415	
Ala Glu Tyr Gln Val Leu Ala Ser Leu Glu Leu Gln Asp Gly Glu Asp			
420	425	430	
Glu Gly Tyr Phe Gln Glu Leu Leu Gly Ser Val Asn Ser Leu Leu Lys			

435
Glu Leu Arg
450

440

445

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 254 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

```

Met Trp Gln Ala Gly Lys Arg Gln Ala Ser Arg Ala Phe Ser Leu Tyr
 1             5             10             15
Ala Asn Ile Asp Ile Leu Arg Pro Tyr Phe Asp Val Glu Pro Ala Gln
      20             25             30
Val Arg Ser Arg Leu Leu Glu Ser Met Ile Pro Ile Lys Met Val Asn
      35             40             45
Phe Pro Gln Lys Ile Ala Gly Glu Leu Tyr Gly Pro Leu Met Leu Val
      50             55             60
Phe Thr Leu Val Ala Ile Leu Leu His Gly Met Lys Thr Ser Asp Thr
      65             70             75             80
Ile Ile Arg Glu Gly Thr Leu Met Gly Thr Ala Ile Gly Thr Cys Phe
      85             90             95
Gly Tyr Trp Leu Gly Val Ser Ser Phe Ile Tyr Phe Leu Ala Tyr Leu
      100            105            110
Cys Asn Ala Gln Ile Thr Met Leu Gln Met Leu Ala Leu Leu Gly Tyr
      115            120            125
Gly Leu Phe Gly His Cys Ile Val Leu Phe Ile Thr Tyr Asn Ile His
      130            135            140
Leu His Ala Leu Phe Tyr Leu Phe Trp Leu Leu Val Gly Gly Leu Ser
      145            150            155            160

```

Thr Leu Arg Met Val Ala Val Leu Val Ser Arg Thr Val Gly Pro Thr
 165 170 175
 Gln Arg Leu Leu Leu Cys Gly Thr Leu Ala Ala Leu His Met Leu Phe
 180 185 190
 Leu Leu Tyr Leu His Phe Ala Tyr His Lys Val Val Glu Gly Ile Leu
 195 200 205
 Asp Thr Leu Glu Gly Pro Asn Ile Pro Pro Ile Gln Arg Val Pro Arg
 210 215 220
 Asp Ile Pro Ala Met Leu Pro Ala Ala Arg Leu Pro Thr Thr Val Leu
 225 230 235 240
 Asn Ala Thr Ala Lys Ala Val Ala Val Thr Leu Gln Ser His
 245 250

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 221 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Met Gly Ser Glu Asn Glu Ala Leu Asp Leu Ser Met Lys Ser Val Pro
 1 5 10 15
 Trp Leu Lys Ala Gly Glu Val Ser Pro Pro Ile Phe Gln Glu Asp Ala
 20 25 30
 Ala Leu Asp Leu Ser Val Ala Ala His Arg Lys Ser Glu Pro Pro Pro
 35 40 45
 Glu Thr Leu Tyr Asp Ser Gly Ala Ser Val Asp Ser Ser Gly His Thr
 50 55 60
 Val Met Glu Lys Leu Pro Ser Gly Met Glu Ile Ser Phe Ala Pro Ala
 65 70 75 80
 Thr Ser His Glu Ala Pro Ala Met Met Asp Ser His Ile Ser Ser Ser

	85	90	95
Asp Ala Ala Thr Glu Met Leu Ser Gln Pro Asn His Pro Ser Gly Glu			
100	105	110	
Val Lys Ala Glu Asn Asn Ile Glu Met Val Gly Glu Ser Gln Ala Ala			
115	120	125	
Lys Val Ile Val Ser Val Glu Asp Ala Val Pro Thr Ile Phe Cys Gly			
130	135	140	
Lys Ile Lys Gly Leu Ser Gly Val Ser Thr Lys Asn Phe Ser Phe Lys			
145	150	155	160
Arg Glu Asp Ser Val Leu Gln Gly Tyr Asp Ile Asn Ser Gln Gly Glu			
165	170	175	
Glu Ser Met Gly Asn Ala Glu Pro Leu Arg Lys Pro Ile Lys Asn Arg			
180	185	190	
Ser Ile Lys Leu Lys Lys Val Asn Ser Gln Glu Val His Met Leu Pro			
195	200	205	
Ile Lys Lys Gln Arg Leu Ala Thr Phe Phe Pro Arg Lys			
210	215	220	

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 266 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

Met Val Lys Val Thr Phe Asn Ser Ala Leu Ala Gln Lys Glu Ala Lys			
1	5	10	15
Lys Asp Glu Pro Lys Ser Gly Glu Glu Ala Leu Ile Ile Pro Pro Asp			
20	25	30	
Ala Val Ala Val Asp Cys Lys Asp Pro Asp Asp Val Val Pro Val Gly			
35	40	45	

Gln Arg Arg Ala Trp Cys Trp Cys Met Cys Phe Gly Leu Ala Phe Met
 50 55 60
 Leu Ala Gly Val Ile Leu Gly Gly Ala Tyr Leu Tyr Lys Tyr Phe Ala
 65 70 75 80
 Leu Gln Pro Asp Asp Val Tyr Tyr Cys Gly Ile Lys Tyr Ile Lys Asp
 85 90 95
 Asp Val Ile Leu Asn Glu Pro Ser Ala Asp Ala Pro Ala Ala Leu Tyr
 100 105 110
 Gln Thr Ile Glu Glu Asn Ile Lys Ile Phe Glu Glu Glu Glu Val Glu
 115 120 125
 Phe Ile Ser Val Pro Val Pro Glu Phe Ala Asp Ser Asp Pro Ala Asn
 130 135 140
 Ile Val His Asp Phe Asn Lys Lys Leu Thr Ala Tyr Leu Asp Leu Asn
 145 150 155 160
 Leu Asp Lys Cys Tyr Val Ile Pro Leu Asn Thr Ser Ile Val Met Pro
 165 170 175
 Pro Arg Asn Leu Leu Glu Leu Leu Ile Asn Ile Lys Ala Gly Thr Tyr
 180 185 190
 Leu Pro Gln Ser Tyr Leu Ile His Glu His Met Val Ile Thr Asp Arg
 195 200 205
 Ile Glu Asn Ile Asp His Leu Gly Phe Phe Ile Tyr Arg Leu Cys His
 210 215 220
 Asp Lys Glu Thr Tyr Lys Leu Gln Arg Arg Glu Thr Ile Lys Gly Ile
 225 230 235 240
 Gln Lys Arg Glu Ala Ser Asn Cys Phe Ala Ile Arg His Phe Glu Asn
 245 250 255
 Lys Phe Ala Val Glu Thr Leu Ile Cys Ser
 260 265

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 251 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

```

Met Pro Thr Gly Asp Phe Asp Ser Lys Pro Ser Trp Ala Asp Gln Val
 1           5           10           15
Glu Glu Glu Gly Glu Asp Asp Lys Cys Val Thr Ser Glu Leu Leu Lys
      20           25           30
Gly Ile Pro Leu Ala Thr Gly Asp Thr Ser Pro Glu Pro Glu Leu Leu
      35           40           45
Pro Gly Ala Pro Leu Pro Pro Pro Lys Glu Val Ile Asn Gly Asn Ile
      50           55           60
Lys Thr Val Thr Glu Tyr Lys Ile Asp Glu Asp Gly Lys Lys Phe Lys
65           70           75           80
Ile Val Arg Thr Phe Arg Ile Glu Thr Arg Lys Ala Ser Lys Ala Val
      85           90           95
Ala Arg Arg Lys Asn Trp Lys Lys Phe Gly Asn Ser Glu Phe Asp Pro
      100          105          110
Pro Gly Pro Asn Val Ala Thr Thr Thr Val Ser Asp Asp Val Ser Met
      115          120          125
Thr Phe Ile Thr Ser Lys Glu Asp Leu Asn Cys Gln Glu Glu Glu Asp
      130          135          140
Pro Met Asn Lys Phe Lys Gly Gln Lys Ile Val Ser Cys Arg Ile Cys
145          150          155          160
Lys Gly Asp His Trp Thr Thr Arg Cys Pro Tyr Lys Asp Thr Leu Gly
      165          170          175
Pro Met Gln Lys Glu Leu Ala Glu Gln Leu Gly Leu Ser Thr Gly Glu
      180          185          190
Lys Glu Lys Leu Pro Gly Glu Leu Glu Pro Val Gln Ala Thr Gln Asn
      195          200          205
Lys Thr Gly Lys Tyr Val Pro Pro Ser Leu Arg Asp Gly Ala Ser Arg
      210          215          220
Arg Gly Glu Ser Met Gln Pro Asn Arg Arg Ala Asp Asp Asn Ala Thr
225          230          235          240
Ile Arg Val Thr Asn Leu Arg Arg Gly His Ala
      245          250

```

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 377 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

```

Met Arg Arg Leu Asn Arg Lys Lys Thr Leu Ser Leu Val Lys Glu Leu
 1             5             10             15
Asp Ala Phe Pro Lys Val Pro Glu Ser Tyr Val Glu Thr Ser Ala Ser
      20             25             30
Gly Gly Thr Val Ser Leu Ile Ala Phe Thr Thr Met Ala Leu Leu Thr
      35             40             45
Ile Met Glu Phe Ser Val Tyr Gln Asp Thr Trp Met Lys Tyr Glu Tyr
      50             55             60
Glu Val Asp Lys Asp Phe Ser Ser Lys Leu Arg Ile Asn Ile Asp Ile
      65             70             75             80
Thr Val Ala Met Lys Cys Gln Tyr Val Gly Ala Asp Val Leu Asp Leu
      85             90             95
Ala Glu Thr Met Val Ala Ser Ala Asp Gly Leu Val Tyr Glu Pro Thr
      100            105            110
Val Phe Asp Leu Ser Pro Gln Gln Lys Glu Trp Gln Arg Met Leu Gln
      115            120            125
Leu Ile Gln Ser Arg Leu Gln Glu Glu His Ser Leu Gln Asp Val Ile
      130            135            140
Phe Lys Ser Ala Phe Lys Ser Thr Ser Thr Ala Leu Pro Pro Arg Glu
      145            150            155            160
Asp Asp Ser Ser Gln Ser Pro Asn Ala Cys Arg Ile His Gly His Leu
      165            170            175
Tyr Val Asn Lys Val Ala Gly Asn Phe His Ile Thr Val Gly Lys Ala
      180            185            190

```


Ile Pro His Pro Arg Gly His Ala His Leu Ala Ala Leu Val Asn His
 195 200 205
 Glu Ser Tyr Asn Phe Ser His Arg Ile Asp His Leu Ser Phe Gly Glu
 210 215 220
 Leu Val Pro Ala Ile Ile Asn Pro Leu Asp Gly Thr Glu Lys Ile Ala
 225 230 235 240
 Ile Asp His Asn Gln Met Phe Gln Tyr Phe Ile Thr Val Val Pro Thr
 245 250 255
 Lys Leu His Thr Tyr Lys Ile Ser Ala Asp Thr His Gln Phe Ser Val
 260 265 270
 Thr Glu Arg Glu Arg Ile Ile Asn His Ala Ala Gly Ser His Gly Val
 275 280 285
 Ser Gly Ile Phe Met Lys Tyr Asp Leu Ser Ser Leu Met Val Thr Val
 290 295 300
 Thr Glu Glu His Met Pro Phe Trp Gln Phe Phe Val Arg Leu Cys Gly
 305 310 315 320
 Ile Val Gly Gly Ile Phe Ser Thr Thr Gly Met Leu His Gly Ile Gly
 325 330 335
 Lys Phe Ile Val Glu Ile Ile Cys Cys Arg Phe Arg Leu Gly Ser Tyr
 340 345 350
 Lys Pro Val Asn Ser Val Pro Phe Glu Asp Gly His Thr Asp Asn His
 355 360 365
 Leu Pro Leu Leu Glu Asn Asn Thr His
 370 375

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 250 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

Met Gly Ser Gln His Ser Ala Ala Ala Arg Pro Ser Ser Cys Arg Arg
 1 5 10 15
 Lys Gln Glu Asp Asp Arg Asp Gly Leu Leu Ala Glu Arg Glu Gln Glu
 20 25 30
 Glu Ala Ile Ala Gln Phe Pro Tyr Val Glu Phe Thr Gly Arg Asp Ser
 35 40 45
 Ile Thr Cys Leu Thr Cys Gln Gly Thr Gly Tyr Ile Pro Thr Glu Gln
 50 55 60
 Val Asn Glu Leu Val Ala Leu Ile Pro His Ser Asp Gln Arg Leu Arg
 65 70 75 80
 Pro Gln Arg Thr Lys Gln Tyr Val Leu Leu Ser Ile Leu Leu Cys Leu
 85 90 95
 Leu Ala Ser Gly Leu Val Val Phe Phe Leu Phe Pro His Ser Val Leu
 100 105 110
 Val Asp Asp Asp Gly Ile Lys Val Val Lys Val Thr Phe Asn Lys Gln
 115 120 125
 Asp Ser Leu Val Ile Leu Thr Ile Met Ala Thr Leu Lys Ile Arg Asn
 130 135 140
 Ser Asn Phe Tyr Thr Val Ala Val Thr Ser Leu Ser Ser Gln Ile Gln
 145 150 155 160
 Tyr Met Asn Thr Val Val Ser Thr Tyr Val Thr Thr Asn Val Ser Leu
 165 170 175
 Ile Pro Pro Arg Ser Glu Gln Leu Val Asn Phe Thr Gly Lys Ala Glu
 180 185 190
 Met Gly Gly Pro Phe Ser Tyr Val Tyr Phe Phe Cys Thr Val Pro Glu
 195 200 205
 Ile Leu Val His Asn Ile Val Ile Phe Met Arg Thr Ser Val Lys Ile
 210 215 220
 Ser Tyr Ile Gly Leu Met Thr Gln Ser Ser Leu Glu Thr His His Tyr
 225 230 235 240
 Val Asp Cys Gly Gly Asn Ser Thr Ala Ile
 245 250

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 374 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

```

Met Val Thr Cys Phe His Val Pro Tyr Ser Ala Leu Thr Met Phe Ile
 1             5             10             15
Ser Thr Glu Gln Thr Glu Arg Asp Ser Ala Thr Ala Tyr Arg Met Thr
      20             25             30
Val Glu Val Leu Gly Thr Val Leu Gly Thr Ala Ile Gln Gly Gln Ile
      35             40             45
Val Gly Gln Ala Asp Thr Pro Cys Phe Gln Asp Leu Asn Ser Ser Thr
      50             55             60
Val Ala Ser Gln Ser Ala Asn His Thr His Gly Thr Thr Ser His Arg
      65             70             75             80
Glu Thr Gln Lys Ala Tyr Leu Leu Ala Ala Gly Val Ile Val Cys Ile
      85             90             95
Tyr Ile Ile Cys Ala Val Ile Leu Ile Leu Gly Val Arg Glu Gln Arg
      100            105            110
Glu Pro Tyr Glu Ala Gln Gln Ser Glu Pro Ile Ala Tyr Phe Arg Gly
      115            120            125
Leu Arg Leu Val Met Ser His Gly Pro Tyr Ile Lys Leu Ile Thr Gly
      130            135            140
Phe Leu Phe Thr Ser Leu Ala Phe Met Leu Val Glu Gly Asn Phe Val
      145            150            155            160
Leu Phe Cys Thr Tyr Thr Leu Gly Phe Arg Asn Glu Phe Gln Asn Leu
      165            170            175
Leu Leu Ala Ile Met Leu Ser Ala Thr Leu Thr Ile Pro Ile Trp Gln
      180            185            190
Trp Phe Leu Thr Arg Phe Gly Lys Lys Thr Ala Val Tyr Val Gly Ile
      195            200            205
Ser Ser Ala Val Pro Phe Leu Ile Leu Val Ala Leu Met Glu Ser Asn

```

(2) INFORMATION FOR SEQ ID NO:34:

(A) LENGTH: 334 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

66

Gly Gln Val Leu Ala Gly Arg Ala Arg Arg Leu Leu Leu Gln Phe Gly
 20 25 30
 Val Leu Phe Cys Thr Ile Leu Leu Leu Leu Trp Val Ser Val Phe Leu
 35 40 45
 Tyr Gly Ser Phe Tyr Tyr Ser Tyr Met Pro Thr Val Ser His Leu Ser
 50 55 60
 Pro Val His Phe Tyr Tyr Arg Thr Asp Cys Asp Ser Ser Thr Thr Ser
 65 70 75 80
 Leu Cys Ser Phe Pro Val Ala Asn Val Ser Leu Thr Lys Gly Gly Arg
 85 90 95
 Asp Arg Val Leu Met Tyr Gly Gln Pro Tyr Arg Val Thr Leu Glu Leu
 100 105 110
 Glu Leu Pro Glu Ser Pro Val Asn Gln Asp Leu Gly Met Phe Leu Val
 115 120 125
 Thr Ile Ser Cys Tyr Thr Arg Gly Gly Arg Ile Ile Ser Thr Ser Ser
 130 135 140
 Arg Ser Val Met Leu His Tyr Arg Ser Asp Leu Leu Gln Met Leu Asp
 145 150 155 160
 Thr Leu Val Phe Ser Ser Leu Leu Leu Phe Gly Phe Ala Glu Gln Lys
 165 170 175
 Gln Leu Leu Glu Val Glu Leu Tyr Ala Asp Tyr Arg Glu Asn Ser Tyr
 180 185 190
 Val Pro Thr Thr Gly Ala Ile Ile Glu Ile His Ser Lys Arg Ile Gln
 195 200 205
 Leu Tyr Gly Ala Tyr Leu Arg Ile His Ala His Phe Thr Gly Leu Arg
 210 215 220
 Tyr Leu Leu Tyr Asn Phe Pro Met Thr Cys Ala Phe Ile Gly Val Ala
 225 230 235 240
 Ser Asn Phe Thr Phe Leu Ser Val Ile Val Leu Phe Ser Tyr Met Gln
 245 250 255
 Trp Val Trp Gly Gly Ile Trp Pro Arg His Arg Phe Ser Leu Gln Val
 260 265 270
 Asn Ile Arg Lys Arg Asp Asn Ser Arg Lys Glu Val Gln Arg Arg Ile
 275 280 285
 Ser Ala His Gln Pro Gly Pro Glu Gly Gln Glu Glu Ser Thr Pro Gln
 290 295 300

Ser Asp Val Thr Glu Asp Gly Glu Ser Pro Glu Asp Pro Ser Gly Thr
 305 310 315 320
 Glu Val Ser Cys Pro Arg Arg Arg Asn Gln Ile Ser Ser Pro
 325 330

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 276 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

Met Thr His Pro Gly Thr Gly Asp Ile Ile Ala Val Met Ile Thr Glu
 1 5 10 15
 Leu Arg Gly Lys Asp Ile Leu Ser Tyr Leu Glu Lys Asn Ile Ser Val
 20 25 30
 Gln Met Thr Ile Ala Val Gly Thr Arg Met Pro Pro Lys Asn Phe Ser
 35 40 45
 Arg Gly Ser Leu Val Phe Val Ser Ile Ser Phe Ile Val Leu Met Ile
 50 55 60
 Ile Ser Ser Ala Trp Leu Ile Phe Tyr Phe Ile Gln Lys Ile Arg Tyr
 65 70 75 80
 Thr Asn Ala Arg Asp Arg Asn Gln Arg Arg Leu Gly Asp Ala Ala Lys
 85 90 95
 Lys Ala Ile Ser Lys Leu Thr Thr Arg Thr Val Lys Lys Gly Asp Lys
 100 105 110
 Glu Thr Asp Pro Asp Phe Asp His Cys Ala Val Cys Ile Glu Ser Tyr
 115 120 125
 Lys Gln Asn Asp Val Val Arg Ile Leu Pro Cys Lys His Val Phe His
 130 135 140
 Lys Ser Cys Val Asp Pro Trp Leu Ser Glu His Cys Thr Cys Pro Met

145	150	155	160
Cys Lys Leu Asn Ile Leu Lys Ala Leu Gly Ile Val Pro Asn Leu Pro			
	165	170	175
Cys Thr Asp Asn Val Ala Phe Asp Met Glu Arg Leu Thr Arg Thr Gln			
	180	185	190
Ala Val Asn Arg Arg Ser Ala Leu Gly Asp Leu Ala Gly Asp Asn Ser			
	195	200	205
Leu Gly Leu Glu Pro Leu Arg Thr Ser Gly Ile Ser Pro Leu Pro Gln			
	210	215	220
Asp Gly Glu Leu Thr Pro Arg Thr Gly Glu Ile Asn Ile Ala Val Thr			
	225	230	235
Lys Glu Trp Phe Ile Ile Ala Ser Phe Gly Leu Leu Ser Ala Leu Thr			
	245	250	255
Leu Cys Tyr Met Ile Ile Arg Ala Thr Ala Ser Leu Asn Ala Asn Glu			
	260	265	270
Val Glu Trp Phe			
	275		

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 210 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Met	Ala	Asn	Ser	Gly	Leu	Gln	Leu	Leu	Gly	Phe	Ser	Met	Ala	Leu	Leu
1					5				10					15	
Gly	Trp	Val	Gly	Leu	Val	Ala	Cys	Thr	Ala	Ile	Pro	Gln	Trp	Gln	Met
		20						25					30		
Ser	Ser	Tyr	Ala	Gly	Asp	Asn	Ile	Ile	Thr	Ala	Gln	Ala	Met	Tyr	Lys
		35						40					45		

Gly Leu Trp Met Asp Cys Val Thr Gln Ser Thr Gly Met Met Ser Cys
 50 55 60
 Lys Met Tyr Asp Ser Val Leu Ala Leu Ser Ala Ala Leu Gln Ala Thr
 65 70 75 80
 Arg Ala Leu Met Val Val Ser Leu Val Leu Gly Phe Leu Ala Met Phe
 85 90 95
 Val Ala Thr Met Gly Met Lys Cys Thr Arg Cys Gly Gly Asp Asp Lys
 100 105 110
 Val Lys Lys Ala Arg Ile Ala Met Gly Gly Gly Ile Ile Phe Ile Val
 115 120 125
 Ala Gly Leu Ala Ala Leu Val Ala Cys Ser Trp Tyr Gly His Gln Ile
 130 135 140
 Val Thr Asp Phe Tyr Asn Pro Leu Ile Pro Thr Asn Ile Lys Tyr Glu
 145 150 155 160
 Phe Gly Pro Ala Ile Phe Ile Gly Trp Ala Gly Ser Ala Leu Val Ile
 165 170 175
 Leu Gly Gly Ala Leu Leu Ser Cys Ser Cys Pro Gly Asn Glu Ser Lys
 180 185 190
 Ala Gly Tyr Arg Ala Pro Arg Ser Tyr Pro Lys Ser Asn Ser Ser Lys
 195 200 205
 Glu Tyr
 210

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 476 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Met Ile Arg Pro Gln Leu Arg Thr Ala Gly Leu Gly Arg Cys Leu Leu

1	5	10	15
Pro Gly Leu	Leu Leu Leu Val	Pro Val Leu Trp	Ala Gly Ala Glu
20	25	30	
Lys Leu His	Thr Gln Pro Ser Cys	Pro Ala Val Cys	Gln Pro Thr Arg
35	40	45	
Cys Pro Ala	Leu Pro Thr Cys	Ala Leu Gly Thr	Thr Pro Val Phe Asp
50	55	60	
Leu Cys Arg	Cys Cys Arg Val	Cys Pro Ala Ala	Glu Arg Glu Val Cys
65	70	75	80
Gly Gly Ala	Gln Gly Gln Pro	Cys Ala Pro Gly	Leu Gln Cys Leu Gln
85	90	95	
Pro Leu Arg	Pro Gly Phe Pro	Ser Thr Cys Gly	Cys Pro Thr Leu Gly
100	105	110	
Gly Ala Val	Cys Gly Ser Asp	Arg Arg Thr Tyr	Pro Ser Met Cys Ala
115	120	125	
Leu Arg Ala	Glu Asn Arg Ala	Ala Arg Arg Leu	Gly Lys Val Pro Ala
130	135	140	
Val Pro Val	Gln Trp Gly Asn	Cys Gly Asp Thr	Gly Thr Arg Ser Ala
145	150	155	160
Gly Pro Leu	Arg Arg Asn Tyr	Asn Phe Ile Ala	Ala Val Val Glu Lys
165	170	175	
Val Ala Pro	Ser Val Val His	Val Gln Leu Trp	Gly Arg Leu Leu His
180	185	190	
Gly Ser Arg	Leu Val Pro Val	Tyr Ser Gly Ser	Gly Phe Ile Val Ser
195	200	205	
Glu Asp Gly	Leu Ile Ile Thr	Asn Ala His Val	Val Arg Asn Gln Gln
210	215	220	
Trp Ile Glu	Val Val Leu Gln	Asn Gly Ala Arg	Tyr Glu Ala Val Val
225	230	235	240
Lys Asp Ile	Asp Leu Lys Leu	Asp Leu Ala Val	Ile Lys Ile Glu Ser
245	250	255	
Asn Ala Glu	Leu Pro Val Leu	Met Leu Gly Arg	Ser Ser Asp Leu Arg
260	265	270	
Ala Gly Glu	Phe Val Val Ala	Leu Gly Ser Pro	Phe Ser Leu Gln Asn
275	280	285	
Thr Ala Thr	Ala Gly Ile Val	Ser Thr Lys Gln	Arg Gly Gly Lys Glu

290	295	300
Leu Gly Met Lys Asp Ser Asp Met Asp Tyr Val Gln Ile Asp Ala Thr		
305	310	315
Ile Asn Tyr Gly Asn Ser Gly Gly Pro Leu Val Asn Leu Asp Gly Asp		320
	325	330
Val Ile Gly Val Asn Ser Leu Arg Val Thr Asp Gly Ile Ser Phe Ala		335
	340	345
Ile Pro Ser Asp Arg Val Arg Gln Phe Leu Ala Glu Tyr His Glu His		350
	355	360
Gln Met Lys Gly Lys Ala Phe Ser Asn Lys Lys Tyr Leu Gly Leu Gln		365
	370	375
Met Leu Ser Leu Thr Val Pro Leu Ser Glu Glu Leu Lys Met His Tyr		380
385	390	395
Pro Asp Phe Pro Asp Val Ser Ser Gly Val Tyr Val Cys Lys Val Val		400
	405	410
Glu Gly Thr Ala Ala Gln Ser Ser Gly Leu Arg Asp His Asp Val Ile		415
	420	425
Val Asn Ile Asn Gly Lys Pro Ile Thr Thr Thr Thr Asp Val Val Lys		430
	435	440
Ala Leu Asp Ser Asp Ser Leu Ser Met Ala Val Leu Arg Gly Lys Asp		445
	450	455
Asn Leu Leu Leu Thr Val Ile Pro Glu Thr Ile Asn		460
465	470	475

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 266 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: None

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

Met Val Lys Val Thr Phe Asn Ser Ala Leu Ala Gln Lys Glu Ala Lys
 1 5 10 15
 Lys Asp Glu Pro Glu Ser Gly Glu Glu Ala Leu Ile Ile Pro Pro Asp
 20 25 30
 Ala Val Ala Val Asp Cys Lys Asp Pro Asp Asp Val Val Pro Val Gly
 35 40 45
 Gln Arg Arg Ala Trp Cys Trp Cys Met Cys Phe Gly Leu Ala Phe Met
 50 55 60
 Leu Ala Gly Val Ile Leu Gly Gly Ala Tyr Leu Tyr Lys Tyr Phe Ala
 65 70 75 80
 Leu Gln Pro Asp Asp Val Tyr Tyr Cys Gly Ile Lys Tyr Ile Lys Asp
 85 90 95
 Asp Val Ile Leu Asn Glu Pro Ser Ala Asp Ala Pro Ala Ala Leu Tyr
 100 105 110
 Gln Thr Ile Glu Glu Asn Ile Lys Ile Phe Glu Glu Glu Glu Val Glu
 115 120 125
 Phe Ile Ser Val Pro Val Pro Glu Phe Ala Asp Ser Asp Pro Ala Asn
 130 135 140
 Ile Val His Asp Phe Asn Lys Lys Leu Thr Ala Tyr Leu Asp Leu Asn
 145 150 155 160
 Leu Asp Lys Cys Tyr Val Ile Pro Leu Asn Thr Ser Ile Val Met Pro
 165 170 175
 Pro Arg Asn Leu Leu Glu Leu Leu Ile Asn Ile Lys Ala Gly Thr Tyr
 180 185 190
 Leu Pro Gln Ser Tyr Leu Ile His Glu His Met Val Ile Thr Asp Arg
 195 200 205
 Ile Glu Asn Ile Asp His Leu Gly Phe Phe Ile Tyr Arg Leu Cys His
 210 215 220
 Asp Lys Glu Thr Tyr Lys Leu Gln Arg Arg Glu Thr Ile Lys Gly Ile
 225 230 235 240
 Gln Lys Arg Glu Ala Ser Asn Cys Phe Ala Ile Arg His Phe Glu Asn
 245 250 255
 Lys Phe Ala Val Glu Thr Leu Ile Cys Ser
 260 265

We Claim:

1. An isolated and purified human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

2. An isolated and purified human protein having an amino acid sequence which is at least 85% identical to an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

3. An isolated and purified human polypeptide comprising at least 6 contiguous amino acids of an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

4. A fusion protein comprising a first protein segment and a second protein segment fused together by means of a peptide bond, wherein the first protein segment consists of at least 6 contiguous amino acids selected from the group consisting of the amino acid sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38.

5. A preparation of antibodies which specifically bind to the human protein of claim 1.

6. An isolated and purified subgenomic polynucleotide having a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

7. An isolated gene corresponding to a cDNA sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19.

8. A DNA construct for expressing all or a portion of a human protein having an amino acid sequence selected from the group consisting of the amino acid

sequences shown in SEQ ID Nos:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, comprising:

a promoter; and

a polynucleotide segment encoding at least 6 contiguous amino acids of the human protein, wherein the polynucleotide segment is located downstream from the promoter, wherein transcription of the polynucleotide segment initiates at or 3' to the promoter.

9. A host cell comprising a DNA construct comprising:

a promoter; and

a polynucleotide segment encoding at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the group consisting of the amino acid sequences shown in SEQ ID NOs:20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, and 38, wherein the polynucleotide segment is located downstream from the promoter and wherein transcription of the polynucleotide segment initiates at or 3' to the promoter.

10. A homologously recombinant cell having incorporated therein a new transcription initiation unit, wherein the new transcription initiation unit comprises in 5' to 3' order:

(a) an exogenous regulatory sequence;

(b) an exogenous exon; and

(c) a splice donor site,

wherein the transcription initiation unit is located upstream to a coding sequence of a gene, wherein the gene comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences shown in SEQ ID NOs:1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, and 19 and wherein the exogenous regulatory sequence controls transcription of the coding sequence of the gene.

11. A method of producing a human protein, comprising the steps of:

growing a culture of a cell comprising a DNA construct comprising

(1) a promoter and (2) a polynucleotide segment encoding at least 6 contiguous amino acids of a human protein having an amino acid sequence selected from the

5

12. A method of producing a human protein, comprising the steps of:

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- 15

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comparing the first population of polypeptides with the second population of polypeptides; and

detecting polypeptide members of the second population which have been modified by the rough microsomes.





INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : C12N 15/12, 15/62, 15/85, 5/10, 1/21, C07K 14/47, 16/18	A3	(11) International Publication Number: WO 98/25959 (43) International Publication Date: 18 June 1998 (18.06.98)
(21) International Application Number: PCT/US97/22787 (22) International Filing Date: 11 December 1997 (11.12.97) (30) Priority Data: 60/032,757 11 December 1996 (11.12.96) US (71) Applicant: CHIRON CORPORATION [US/US]; 4560 Horton Street, Emeryville, CA 94608 (US). (72) Inventors: ESCOBEDO, Jaime; 1470 Livorna Road, Alamo, CA 94507 (US). HU, Quianjin; Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608 (US). GARCIA, Pablo; 882 Chenery Street, San Francisco, CA 94131 (US). WILLIAMS, Lewis, T.; 3 Miraflores Lane, Tibouron, CA 94920 (US). KOTHAKOTA, Srinivas; Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608 (US). (74) Agents: POTTER, Jane, E., R.; Chiron Corporation, Intellectual Property - R440, P.O. Box 8097, Emeryville, CA 94662-8097 (US) et al.		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 8 October 1998 (08.10.98)
(54) Title: SECRETED HUMAN PROTEINS		
(57) Abstract		
<p>Secreted proteins can be identified using a method which exploits the ability of microsomes to modify proteins post-translationally. Nineteen human secreted proteins and full-length cDNA sequences encoding the proteins have been identified using this method. The proteins and cDNA sequences can be used, <i>inter alia</i>, for targeting other proteins to the membrane or extracellular milieu.</p>		

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INTERNATIONAL SEARCH REPORT

Intern. Application No
PCT/83 97/22787

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/12 C12N15/62 C12N15/85 C12N5/10 C12N1/21
C07K14/47 C07K16/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 92 03466 A (US GOVERNMENT) 5 March 1992 see the whole document ---	1-12
A	WO 95 31560 A (TRANSKARYOTIC THERAPIES INC ;TRECO DOUGLAS A (US); HEARTLEIN MICHA) 23 November 1995 cited in the application see the whole document ---	10,12
A	TASHIRO K ET AL: "SIGNAL SEQUENCE TRAP: A CLONING STRATEGY FOR SECRETED PROTEINS AND TYPE I MEMBRANE PROTEINS" SCIENCE, vol. 261, 30 July 1993, pages 600-603, XP000673204 see the whole document ---	1-12
-/--		

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

6 April 1998

Date of mailing of the international search report

28-07-1998

Name and mailing address of the ISA

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Fax: (+31-70) 340-3016

Authorized officer

Kania, T

INTERNATIONAL SEARCH REPORT

Application No
PCT/US 97/22787

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JACOBS K ET AL: "A NOVEL METHOD FOR ISOLATING EUKARYOTIC CDNA CLONES ENCODING SECRETED PROTEINS" JOURNAL OF CELLULAR BIOCHEMISTRY - SUPPLEMENT, vol. 21A, 10 March 1995, page 19 XP002027246 see abstract	1-12
A	<div style="text-align: center;">---</div> KLEIN R. ET AL.: "Selection of genes encoding secreted proteins and receptors" PNAS, U.S.A., vol. 93, no. 14, 9 July 1996, pages 7108-7113, XP002061411 see the whole document <div style="text-align: center;">-----</div>	1-12

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 97/ 22787

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see annex

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

claims 1-12 (partially) (Extra sheet-1)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/

1. Claims: 1-12 partially

An isolated human protein having an amino acid sequence according to SEQ ID No. 20, homologs and fragments thereof, fusion proteins therewith, antibodies thereto.

An isolated and purified polynucleotide having the sequence according to SEQ ID No. 1, the corresponding gene, DNA constructs, host cells, and homologously recombinant cells comprising said polynucleotide.

A method of producing said protein using said DNA sequences, constructs, or cells.

2. Claims: 1-12 partially

idem for SEQ ID 21, 2

3. Claims: 1-12 partially

idem for SEQ ID No. 22, 3

4. Claims: 1-12 partially

idem for SEQ ID No. 23, 4

5. Claims: 1-12 partially

idem for SEQ ID No. 24, 5

6. Claims: 1-12 partially

idem for SEQ ID No. 25, 6

7. Claims: 1-12 partially

idem for SEQ ID No. 26, 7

8. Claims: 1-12 partially

idem for SEQ ID No. 27, 8

9. Claims: 1-12 partially

idem for SEQ ID No. 28, 9

FURTHER INFORMATION CONTINUED FROM PCT/ISA/

10. Claims: 1-12 partially
idem for SEQ ID No. 29, 10
11. Claims: 1-12 partially
idem for SEQ ID No. 30, 11
12. Claims: 1-12 partially
idem for SEQ ID No. 31, 12
13. Claims: 1-12 partially
idem for SEQ ID No. 32, 13
14. Claims: 1-12 partially
idem for SEQ ID No. 33, 14
15. Claims: 1-12 partially
idem for SEQ ID No. 34, 15
16. Claims: 1-12 partially
idem for SEQ ID No. 35, 16
17. Claims: 1-12 partially
idem for SEQ ID No. 36, 17
18. Claims: 1-12 partially
idem for SEQ ID No. 37, 18
19. Claims: 1-12 partially
idem for SEQ ID No. 38, 19

FURTHER INFORMATION CONTINUED FROM PCT/ISA/

20. Claim : 13

A method of identifying a secreted polypeptide which is modified by rough microsomes, comprising:
in vitro transcription of a cDNA population, translation of a first portion in the absence of rough microsomes in vitro, translation of a second portion in the presence of rough microsomes in vitro, comparison of the polypeptides of the first and second portion, and detection of members of the second portion that have been modified by the rough microsomes.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 97/22787

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